In presenting the dissertation as a partial fulfillment of the requirements for an advanced degree from the Georgia Institute of Technology, I agree that the Library of the Institute shall make it available for inspection and circulation in accordance with its regulations governing materials of this type. I agree that permission to copy from, or to publish from, this dissertation may be granted by the professor under whose direction it was written, or, in his absence, by the Dean of the Graduate Division when such copying or publication is solely for scholarly purposes and does not involve potential financial gain. It is understood that any copying from, or publication of, this dissertation which involves potential financial gain will not be allowed without written permission.

7/25/68

ACORENONE-B. A NEW SESQUITERPENE OF THE ACORANE TYPE

A THESIS

Presented to

The Faculty of the Graduate Division

by

Richard James McClure, Jr.

In Partial Fulfillment

of the Requirements for the Degree

Doctor of Philosophy in the

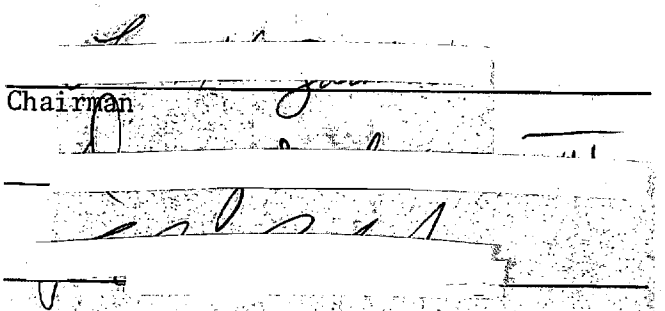
School of Chemistry

Georgia Institute of Technology

November, 1968

ACORENONE-B. A NEW SESQUITERPENE OF THE ACORANE TYPE.

Approved:



Chairman

Date approved by Chairman: November 19, 1968

ACKNOWLEDGMENTS

I wish to express my gratitude to Dr. Leon H. Zalkow for the suggestion of the problem and for his invaluable guidance and counsel during the course of my graduate work and in the preparation of this thesis.

For reading and criticizing this thesis and for his patient guidance and assistance in the solution of the X-ray crystallographic problem, I sincerely thank Dr. J. Aaron Bertrand.

I also thank Dr. Drury S. Caine, III for reading and criticizing this thesis.

In addition, I especially thank my wife, Marjorie, and children, Mark and Brian, for their patience, encouragement, and assitance in helping me toward my goals.

I also thank the National Institutes of Health for financial support during the tenure of my graduate studies.

TABLE OF CONTENTS

Page

LIST OF TABLES

Table | Page

LIST OF FIGURES

LIST OF PLATES

GLOSSARY OF ABBREVIATIONS

Å	angstrom
amu	atomic mass unit(s)
CD	circular dichroism
cps	cycles per second
d	doublet (n.m.r.)
Fo	observed structure factor
Fc	calculated structure factor
GLC	gas-liquid chromatography
H.F.R.	helium flow rate (GLC)
h,k,l	Miller indices
m	multiplet (n.m.r.)
m/e	mass to charge ratio
mg	milligram(s)
min	minute(s)
mol.	molecular
mμ	millimicron
n.m.r.	nuclear magnetic resonance
ORD	optical rotary dispersion
R.T.	retention time (GLC)
s	singlet (n.m.r.)
t	triplet (n.m.r.)
TLC	thin layer chromatography

SUMMARY

A new spiro[4.5]decane sesquiterpene, acorenone-B, has been isolated from a hybrid Bothriochloa intermedia grass. The physical properties and infrared spectrum of acorenone-B (10) were similar to acorenone which was isolated by Herout et al.[5] Interpretation of the n.m.r., infrared, and ultraviolet spectra of acorenone-B (10) provided the structure of the six-membered ring portion of 10 and indicated that the hydrocarbon skeleton was of the acorane, spiro[4.5]decane, type. Direct comparison of dihydroacorenone (12) with dihydroacorenone-B (25) showed that acorenone and acorenone-B were different compounds. Dihydroacorenone-B (25) was reduced to the saturated hydrocarbon 31 via the thioketal 30. The infrared spectra of the hydrocarbons obtained from acorenone-B and acorenone were very similar.

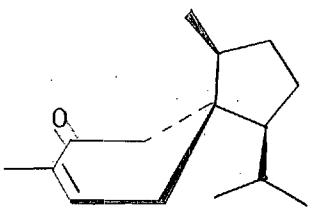
The Baeyer-Villiger oxidation of dihydroacorenone-B (25) yielded a lactone (27) which was reduced with lithium aluminum hydride to give the diol 28. Oxidation of 28, followed by esterification with diazomethane yielded ketoester 29. The presence of a methyl ketone function in 29 confirmed the position of the methyl group on the six-membered ring of acorenone-B (10).

The ozonolysis of acorenone-B (10) yielded diacid 32 which had the same melting point as the diacid obtained from acorenone in a similar manner. The infrared spectrum of the dimethyester of 32 was the same as the infrared spectrum of the dimethylester obtained from acorenone, within the limits imposed by comparing two spectra taken with dif-

ferent spectrophotometers. However, conclusive proof that the two ozonolysis products are identical depends upon a direct comparison of the two products.

Recently Arigoni[20] has provided n.m.r. and infrared spectra of an α,β-unsaturated ketone derived from coccinol (11) which he had assigned the same structure as acorenone-B. Although the spectra of acorenone-B and the coccinol ketone are similar, it is evident from the n.m.r. spectra that they are two different compounds, possibly epimers.

Acorenone-B 4-iodo-2-nitrophenylhydrazone (36) was prepared for the X-ray structure determination of acorenone-B. The crystals were orthorhombic (space group $P2_12_12$) with unit cell dimensions a = 20.81, b = 7.18, c = 14.81 Å; the calculated density for four molecules per unit cell is 1.44 g/cc while the experimentally observed (flotation) value was 1.40 g/cc. The iodine atoms were located by a three-dimensional Patterson and the structure was solved by successive Fourier syntheses. Using full matrix least-squares refinement with isotropic temperature factors and individual layer scale factors, the R index converged to 0.109 for 465 independent non-zero reflections (Mo K_α, precession camera data). A total of 1116 reflections were collected by an automated diffractometer for use in the determination of the absolute configuration of acorenone-B, the R index converged to 0.057 with this data. The absolute configuration of acorenone-B was determined by two methods: Hamilton's R factor significance test and the comparison of Bijvoet pairs. The results of the X-ray analysis have provided the structure and absolute configuration of acorenone-B as depicted in 10. Knowledge of its structure may help to determine the structure of acorenone and coccinol.



10

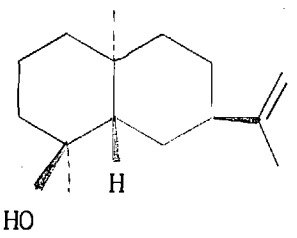
The synthesis of a naturally occurring sesquiterpene with the acorane type of hydrocarbon skeleton has not been reported. The synthesis of acorenone-B has been approached by first constructing the cyclopentane ring portion with the proper constituents. This was accomplished with the Favorskii reaction on pulegone dibromide to give methyl pulegenate. The condensation of methyl pulegeneate with dimethyl carbonate in the presence of sodium hydride yielded diesters 40 and 41. Hydrogenation of 40 or 41 produced diester 42 which had the desired cis relationship of the methyl and isopropyl groups and the diester function could provide the basis for constructing the six-membered ring. However, the condensation reaction went in poor yield so that either more favorable reaction conditions will have to be worked out or the reaction will have to be done on a larger scale to obtain enough material to finish the synthesis of acorenone-B.

CHAPTER I

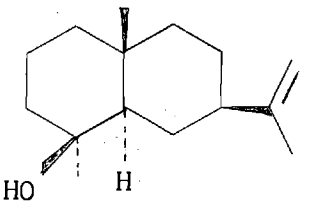
INTRODUCTION

The text of this thesis is concerned with the structure elucidation and partial synthesis of a new sesquiterpene which was isolated from the steam-volatile oil of a hybrid grass, Bothriochloa intermedia, derived from parents of the foothill race Punjab, India and the gangetica race British Guiana.

The grass was provided by the Department of Agronomy at Oklahoma State University. They had obtained and prepared several races of the grass Bothriochloa intermedia in their search for new grasslands. The Agronomy Department was looking for a correlation between palatableness of the grasses and their chemical constituents. The chemical investigation of these grasses was carried out by Dr. Zalkow and his associates and provided several new and interesting sesquiterpenes. The steam-volatile oil of a grass indigenous to India contained a new sesquiterpene, intermedeol[1,2] (1). Another grass indigenous to Malaya contained a similar new sesquiterpene, neointermedeol[3] (2). The new sesquiterpene whose

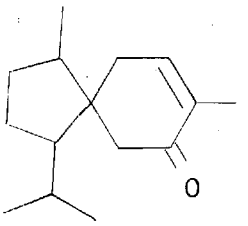


1



2

structure is completely elucidated in this thesis has the gross structure 3, being epimeric with acorenone, which was isolated from sweet-flag oil by Vrkoc and co-workers.[4,5] The name acorenone-B was suggested for the new sesquiterpene to denote its origin. Part of the preliminary structure work on acorenone-B was done by K. Shorno[6] at Oklahoma State University.



3

The field of sesquiterpenes has offered organic chemists many interesting problems. E. J. Corey[7] most elegantly describes the interest in this field in the following quote:

> The virtuosity of nature in the construction of intricate molecules is nowhere more evident than in those families which are described broadly as isoprenoids. Within this group an especially concentrated and impressive display of this synthetic expertise can be found in the sesquiterpene class. Here diverse and unusual arrangements of rings and functionality abound notwithstanding a common origin from the same acyclic C_{15}-precursor, as now seems probable. This remarkable variety of design is perhaps the principal reason for the structural chemist's deep interest in this field of natural products,....

Ruzicka[8] was one of the first chemists to recognize farnesol (4) as the common precursor to all the sesquiterpenes. Ruzicka's rationale for the formation of the cedrene type of sesquiterpenes (5) is given in Figure 1. The biogenesis of sesquiterpenes probably occurs in the plant enzymatically via the pyrophosphate derivative of farnesol;[9] however, Ruzicka's representation is still useful in classifying sesquiterpenes. The scheme

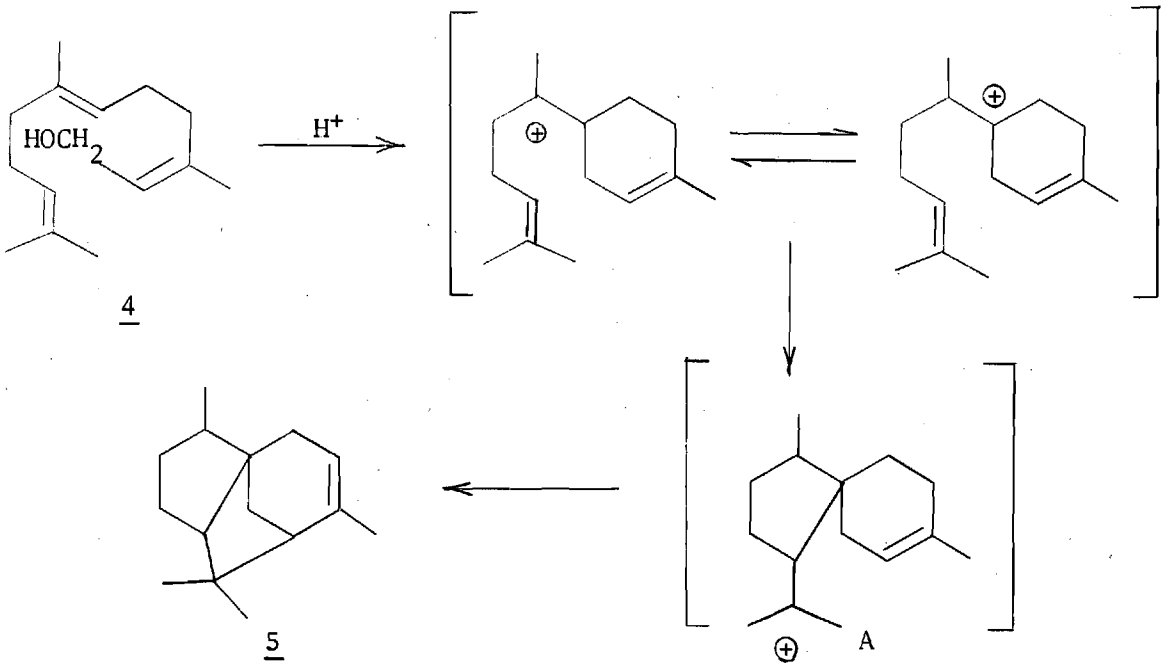
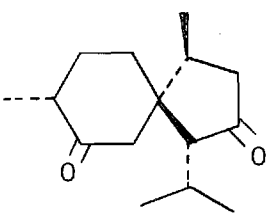


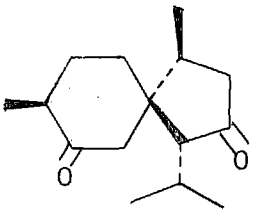
Figure 1. Ruzicka's Biogenetic Scheme to the Cedrene Sesquiterpenes.

is helpful in looking for various structural variations in new sesquiterpenes, for it was three years after Ruzicka's publication that a spirane structure of type A was reported by Sorm[10] for acorone (6). Until recently, there were only five spirane sesquiterpenes reported in the literature, four of them possessing the acorane hydrocarbon skeleton A.

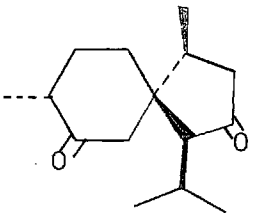
The sesquiterpenes reported to have the acorane type of hydrocarbon skeleton are shown in Figure 2. Acorone[10-18], isoacorone[10-17], and acorenone[4,5] were isolated from sweet-flag oil (Acorus calamus L.) by Sorm et al. The absolute configuration of the methyl group on the cyclohexane ring and the isopropyl group on the cyclopentane ring of 6, 7, and 8 were determined by application of the Hudson-Klyne rule. Dipole moment and optical rotary dispersion measurements were used to assign the absolute configuration of the spirane carbon atom of 6, 7, and 8. However, the correct assignment of the relative stereochemistry of the methyl



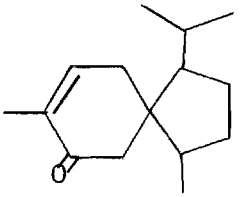
acorone 6



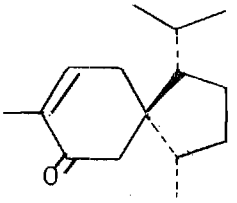
isoacorone 7



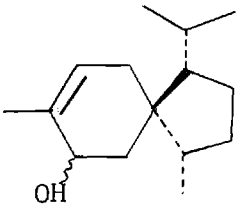
cryptoacorone 8



acorenone 3 (?)



acorenone-B 10



coccinol 11 (?)

Figure 2. Spiro[4.5]decane Sesquiterpenes of the Acorane Type.

group on cyclopentane ring was made by a single crystal X-ray structure determination[18] on the p-bromophenylsulfonylhydrazone derivative of acorone (6), which also confirmed the spirane type hydrocarbon skeleton.

The structure of acorenone was assigned on the basis of the degradation scheme shown in Figure 3. The assignment of the spirane hydrocarbon skeleton was made by comparison of the infrared spectrum of the hydrocarbon 14 with the infrared spectrum of the hydrocarbon obtained from acorone. The position of the carbonyl group in acorenone was assigned on the basis of the isolation of the diacid 15 upon ozonolysis. The stereochemistry of acorenone was not given. A recent book,[19] prefaced by Sorm, has a question mark for the structure of acorenone which indicates that there may be some question about the assigned structure.

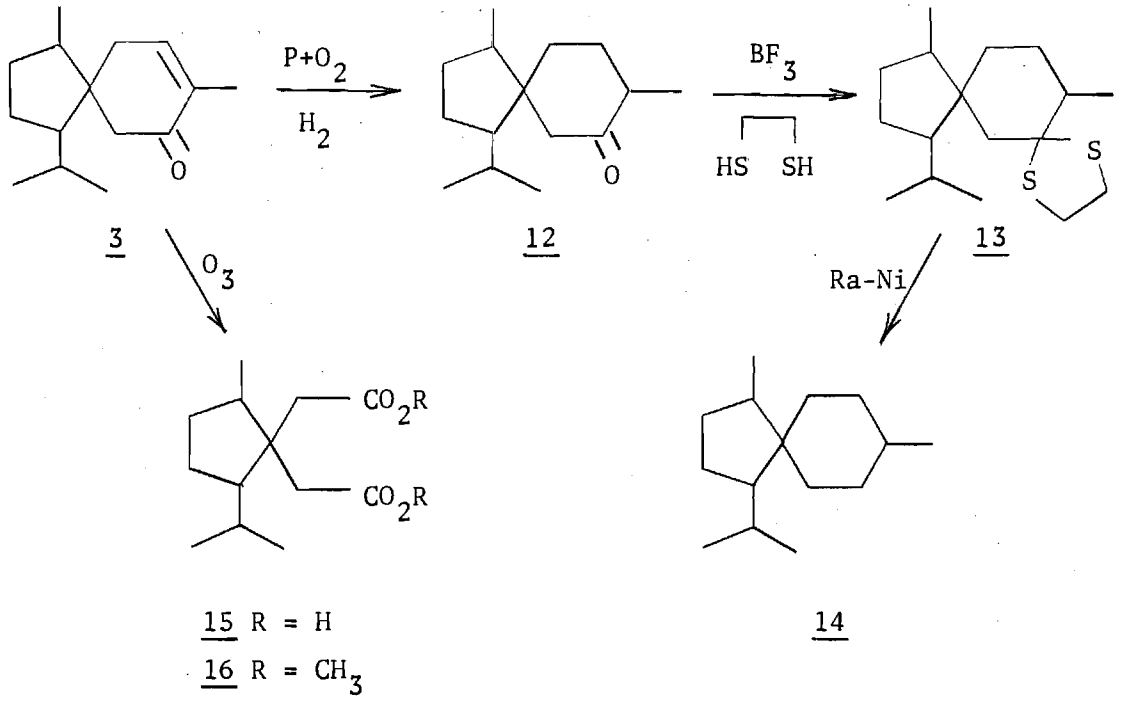
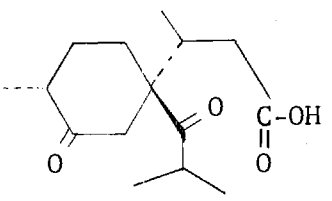


Figure 3. Degradation of Acorenone.

Recently coccinol[20] was isolated from the mycelium of Fusidium coccineum and tentatively assigned structure 11.

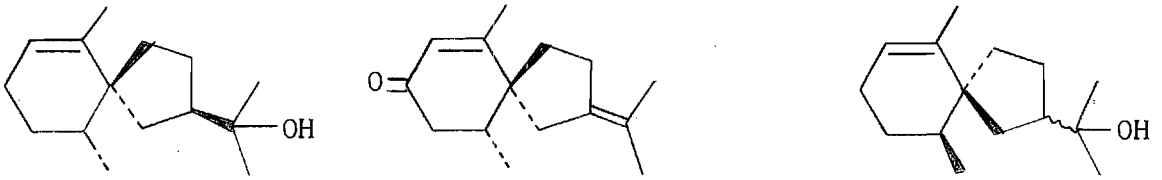
The acidic fraction of the roots of Acorus calamus L. showed some antiepileptic activity.[21] The main constituent of the acidic fraction was acoric acid,[21] assigned structure 17 on the basis of a direct comparison with a degradation product of acorone. Acoric acid is believed to be derived by oxidative fission of the five-membered ring of acorone either biogenetically or by autoxidation.[21]



acoric acid 17

At the present time, there are no reports of a synthesis of naturally occurring sesquiterpene of the acorane type. However, Mellor and Munavalli[22] in a 1964 review article have reported that Parker, Ramage, and Raphael have synthesized acorone, but there has been no subsequent confirmation of this in the literature.

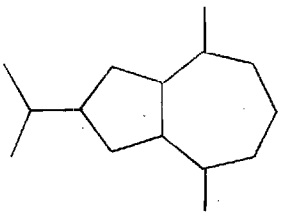
The agarospirane[22] hydrocarbon skeleton was the second type of spiro-sesquiterpene to be isolated. Sesquiterpenes reported to have this type of carbon skeleton are shown in Figure 4. Agarospirol[23] (18) was isolated from infected agarwood (Aquilaria agallocha Roxb). Its structure was supported by degradative studies and by an unambiguous synthesis of a ketone derived from 18. The stereochemistry was tentatively proposed as shown by 18.



agarospirol 18 β-vetivone 19 hinesol 20

Figure 4. Spiro[4.5]decane Sesquiterpenes of the Agarospirane Type.

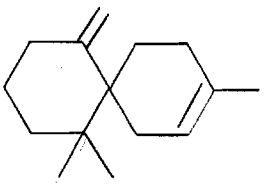
Recently Marshall[24] has shown by synthetic and degradative methods that the entire class of bicyclic vetivane sesquiterpenes (Vetiveria zizanioides) has been erroneously represented[25] by the hydroazulene skeleton 21. Marshall[26] assigned the agarospirane type of structure to β-vetivone (19) on the basis of its degradation to a known spiro[4.5]decane. The absolute configuration of β-vetivone was assigned by a previously[28] reported correlation of β-vetivone to hinesol (20), Marshall suggested



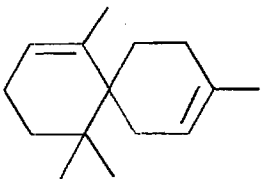
21

that bicyclovetivenol,[29] α-isovetivenene,[30] and β-isovetivenene[30] should be included in the agarospirane class of sesquiterpenes. The synthesis of β-vetivone has been reported.[27]

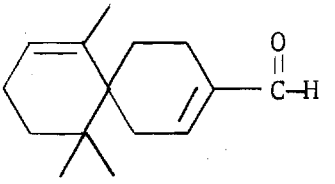
In 1967, chamigrene[31] (22), a spiro[5.5]undecane sesquiterpene, was isolated from the leaf oil of Chamaecyparis taiwanensis. Figure 5 shows the sesquiterpenes reported to have the chamigrene type hydrocarbon skeleton. Recently, α-chamigrene[32] (23) and α-chamigrinal[32] (24) have been reported. Chamigrene has been synthesized.[33]



chamigrene 22



α-chamigrene 23



α-chamigrinal 24

Figure 5. Spiro[5.5]undecane Sesquiterpenes of the Chamigrene Type.

CHAPTER II

INSTRUMENTATION AND EQUIPMENT

Spectral Studies

Nuclear magnetic resonance spectra were obtained using a Varian Associates Model A-60A spectrometer equipped with a spin-decoupler. Tetramethylsilane was used as an internal standard. The abbreviations, s, d, t, q, and m refer to singlet, doublet, triplet, quartet and multiplet respectively.

Mass spectral data were obtained using a Varian Associates Model M 66 mass spectrometer*, or LKB Model 9000 gas chromatograph--single focussing mass spectrometer,** or a consolidated Electrodynamic Corporation Model 21-103C mass spectrometer.***

Infrared spectra were obtained using a Perkin-Elmer Model 237B spectrophotometer or a Beckman IR-5 spectrometer. The spectra of liquids were taken as films formed between two sodium chloride plates; potassium bromide was used in preparing pellets of solid samples for infrared spectra. The band at 1601 cm^{-1} of a polystyrene film (0.05 mm) was used as a reference point.

The optical rotary dispersion, circular dichroism, and ultraviolet spectra were obtained with a Jasco Model ORD/UV-5 spectrophotometer.

---

*These spectra were run by Mr. G. Turner

**These spectra were obtained through the courtesy of Dr. J. Dyer and Dr. C. Sweely.

***These spectra were obtained under the direction of Professor Carl Djerassi.

The optical rotations were determined using either a Rudolph polarimeter or Bellingham and Stanley Model No. 397619 polarimeter equipped with a General Electric Sodium Lab-Arc lamp as the source of the sodium D line.

Physical Separations

Gas-liquid chromatography (GLC) was performed using an F & M Model 400 Biomedical* gas chromatograph with a hydrogen flame detector or an Aerograph Autoprep** Model A-700 gas chromatograph with a thermal detector. Glass columns (6' x 1/4" outside diameter) bent in a U shape were used with the F & M gas chromatograph except as otherwise indicated. Coiled aluminum columns (10' x 1/4") were used with the Aerograph gas chromatograph except as noted. The column temperature (C.T.), helium flow rate (H.F.R.), and the retention time (R_t) are given in the experimental section for each example. The relative peak areas were measured using a Gelman Instruments Co. planimeter or by accurately cutting out the peaks and weighing them on an analytical balance. The column substrates and solid supports used in the GLC analyses were obtained from Applied Science Laboratories or from Hewlett Packard Analytical Instruments.

Thin layer chromatography (TLC) was performed using Silica Gel (according to Stahl, E. Merk AG, Darmstadt, Germany) spread 200 microns thick on 3" x 1" microscope slides. The R_f values were obtained by taking

---

*In the experimental chapter "flame" will be used to denote gas chromatograms obtained with this instrument.

**In the experimental chapter "thermal" will be used to denote gas chromatograms obtained with this instrument.

the ratio of the distance the spot moved to the distance the solvent front moved; detection was with iodine vapor unless otherwise specified.

Column chromatography was carried out using Merck acid washed alumina, activity I, or Silica Gel (0.05-0.2 mm, E. Merck AG, Darmstadt, Germany).

The spinning band distillations were performed with either a Nester/Faust NF-105 micro stainless steel spinning band column or a Nester/Faust NF-135 lab size stainless steel spinning band column.

Miscellaneous

Melting points are uncorrected and were taken on a Thomas-Hoover capillary melting point apparatus or as otherwise indicated. Analyses were performed by Midwest Microlab, Inc., Indianapolis, Indiana or by Alfred Bernhardt Microanalytical Laboratories, Mulheim, West Germany.

Ozonolyses were performed using a Welsbauch Corp. Model T-23 laboratory ozonator as the source of ozone. The rate of production of ozone was determined by passing the gas through an aqueous potassium iodide solution followed by titration of the iodine produced with a standard sodium thiosulfate solution. Diazomethane was generated from EXR-101 obtained from E.I. DuPont Nemours, Inc., Gibbstown, New Jersey.

X-ray Studies

Film Data

The Bragg reflections were recorded photographically on Illford Industrial G X-ray film (5" x 7", cut to 5" x 4-15/16" to fit the film cassett) using a Buerger precession camera with a crystal to film distance of 60 mm.

Zirconium filtered Mo K_α radiation generated by a Picker full-wave X-ray generator was used for the layer photographs. An optical collimator was used to determine the angles between the crystal faces. A microscope equipped with a movable micrometer base was used to obtain the crystal dimensions.

Diffractometer Data

A Picker automated diffractometer with four-circle geometry was used to collect the diffractometer data. The diffractometer was automated by a direct relay to an IBM key punch, through which information was conveyed to and from the diffractometer by punched cards. A NaI (Tl) scintillation detector was used to count the diffracted radiation.

Computations

The Univac 1108 computer was used extensively in the structure determination and the absolute configuration work. The Burroughs B5500 computer was used for the initial computations. An off-line Calcomp plotter, California Computer Products, Inc., was used to plot the molecular structures shown in Figures 9-11.

CHAPTER III

EXPERIMENTAL

Isolation of the Essential Oil of the Hybrid Grass (56 x 627)*

The chopped dry grass was steam distilled in a 12 liter round-bottom flask half-filled with grass so that the grass was tumbled vigorously. The steam distillation was continued until there was no oil in the condensate, which usually required six to ten liters of condensate. The condensate was continuously extracted with ether. The ethereal solution was dried ($MgSO_4$) and the ether removed by distillation at 40° with a Vigreux column to give 0.2% oil based on dry plant. In this manner a total of 120 g of oil collected. GLC analysis (thermal) of the oil (3% PDEAS on 80/100 mesh CW column, C.T. 200°, H.F.R. 50 ml/min) showed one major component with R_t 14.9 min (47.4%) and two minor components with R_t 3.5 min (8.5%) and R_t 6.8 min (9.9%). There were also 12 peaks with R_t 0.2-2.6 min (8.7%) and six peaks with R_t 7.8-11 min (25.5%). The essential oil showed ν_{max}^{KBr} 3450, 3050 (weak), 2925, 2850, 2700 (weak), 1725, and 1675 cm^{-1}.

Isolation of Acorenone-B (10, 1-Isopropyl-4,8-dimethyl-spiro[4.5]dec-8-en-7-one

Column chromatography of the essential oil (20 g) on 500 g of

*The plant material was kindly supplied by Dr. J. Harlan, Agronomy Department, Oklahoma State University and the grasses were grown in Stillwater, Oklahoma. The number 56 represents the year 1956 and 627 indicates the ascension number.

alumina gave 6.7 g (33%) of acorenone-B(10) in the petroleum ether (b.p. 35-40°)-benzene (1:4) eluent. The petroleum ether solvent was purified before using by stirring over concentrated sulfuric acid, distillation, and elution through alumina to remove olefins. The purity of 4.3 g of the eluate was 95 percent and an additional 2.4 g portion was of 99 percent purity by GLC analysis. GLC analysis using conditions identical to those used for analysis of the oil showed that 10 corresponded to the major component of the oil (R_t 14.9 min). The spinning band distillation of 10 (2.4 g) was carried out at a reflux ratio of 20:1 to give pure 10 (1.6 g): n_D^{30} 1.4997, d^{30} 0.9690 g/cc, $[\alpha]_D^{20}$ -13.3 ± 0.1° (neat), b.p. 68°/0.01 mm. GLC analysis (thermal) of 10 (4% PDEAS on 60/80 mesh column, C. T. 190°, H.F.R. 120 ml/min) showed only one peak with R_t 10.1 min. GLC analysis (thermal) of 10 on another column (5% Craig Polyester on 60/80 CW column, C.T. 186°, H.F.R. 50 ml/min) also showed only one peak with R_t 18 min. TLC analysis showed one spot (R_f 0.20, benzene) under a UV lamp and in iodine vapor.

The spectral properties of 10 were as follows: ν_{max}^{film} 1670 cm^{-1} (C = O) (Plate I); λ_{max}^{MeOH} 242 (ε = 16,300), λ_{max}^{MeOH} 310 mμ (ε = 16.5), λ_{max}^{hexane} 236 mμ (ε = 15,000). ORD* of the n → π* transition (c, 0.01499; CH_3OH), 31.3°: $[\Phi]_{589}$ - 1,320°; $[\Phi]_{350}$ + 2,200°; $[\Phi]_{334}$ ± 0°; $[\Phi]_{300}$ shoulder; $[\Phi]_{268}$ - 40,000°. A value for the amplitude of the positive Cotton effect for this case could not be determined due to the

*The convention used in reporting the ORD and CD spectra is that recommended by Dr. P. Crabbe.[34] (See Appendix for the method of calculation). The ORD concentrations are reported in g/100 ml and are indicated by a lower case "c". The CD concentrations are reported in moles/liter and indicated by an upper case "C".

overriding effect of the negative Cotton effect of the $\pi \rightarrow \pi^*$ transition. The ORD of the $n \rightarrow \pi^*$ transition in a nonpolar solvent, hexane, showed the multiplicity usually observed for α,β-unsaturated ketones.[34] CD* of the $n \rightarrow \pi^*$ transition (C, 0.000683; CH_3OH), 34.5°: $[\Theta]_{450} \pm 0$; $[\Theta]_{322}$ + 1,530; $[\Theta]_{255}$ - 2,060; Γ = 39 mμ. ORD of the $\pi \rightarrow \pi^*$ transition (c, 0.0060; CH_3OH), 35.5°: $[\Phi]_{589}$ + 368°; $[\Phi]_{253}$ - 4,950°; $[\Phi]_{240} \pm 0°$; $[\Phi]_{220}$ + 6,600°; $[\Phi]_{216}$ + 2,380°; a = -115. ORD of the $\pi \rightarrow \pi^*$ transition (c, 0.00448; hexane), 34.5°: $[\Phi]_{589}$ + 1,280°; $[\Phi]_{230} \pm 0°$; $[\Phi]_{216}$ + 5,450°; $[\Phi]_{212}$ + 2,720°; a = -96.5. The $\pi \rightarrow \pi^*$ transition of α,β-unsaturated ketones may be solvent dependent[35], so the spectra were run in hexane and methanol. CD of the $\pi \rightarrow \pi^*$ transition (C, 0.000272; CH_3OH), 34.5°: $[\Theta]_{450} \pm 0$; $[\Theta]_{237}$ -7,400; $[\Theta]_{218} \pm 0$; Γ = 23 mμ.

The n.m.r. ($CDCl_3$) of acorenone-B (Plate II) showed signals at 46 (3H, d, CH-$\underline{CH}_3$, J = 6 cps), 52 (3H, d, CH-$\underline{CH}_3$, J = 6 cps), 57 (3H, d, CH-$\underline{CH}_3$, J = 6 cps), 105 (3H, m, C=C-$\underline{CH}_3$), 132 (2H, m, C=C-$\underline{CH}_2$), 124, 141, 155, 172 (2H, doublet of doublets, O=C-$\underline{CH}_2$-C, J = 17 cps, $\Delta^{**}_{\nu AB}$ = 26 cps), and 400 cps (1H, m, C=C-$\underline{H}$). Decoupling experiments indicated that the multiplet at 400 cps changed to a quartet (J = 2 cps) when the multiplet at 132 cps was irradiated (H_1 7.0, DF + 260 cps). The multiplet at 105 cps changed to a triplet (J = 2 cps) when the multiplet at 400 cps was irradiated (H_1 5.0, DF -287 cps). The resolution was not

---

*The convention used in reporting the ORD and CD spectra is that recommended by Dr. P. Crabbe.[34] (See Appendix for the method of calculation). The ORD concentrations are reported in g/100 ml and are indicated by a lower case "c". The CD concentrations are reported in moles/liter and indicated by an upper case "C".

**The method of the calculation of $\Delta_{\nu AB}$ is given in the appendix.

adequate to obtain other decoupling results.

The mass spectrum of acorenone-B (Plate III) gave the parent peak at m/e 220 (82.8%) and the base peak at m/e 135. The precise mass determination of acorenone-B using perfluoroalkane as the reference compound gave M_{220} = 220.178; the molecular weight calculated for the molecular formula $C_{15}H_{24}O$ is 220.183. The only other possible molecular formulas[36] containing carbon, hydrogen, and oxygen in the range of ± 0.01 amu [$C_8H_{28}O_6$, M_{220} + 220.1886 and $C_{11}H_{24}O$ (M_{220} = 220.1674)] could be ruled out based on spectral and chemical evidence.

Anal. Calcd. for $C_{15}H_{24}O$: C, 81.76; H, 10.98
Found: C, 81.53; H, 10.96

Preparation of the 2,4-Dinitrophenylhydrazone of Acorenone-B (10)

Acorenone-B (10, 35 mg) was added to a solution of 2,4-dinitrophenylhydrazine (42 mg) in methanol-concentrated hydrochloric acid (9:1, 2.7 ml) and heated on a steam bath for one minute. Acorenone-B 2,4-dinitrophenylhydrazone was recrystallized from ethanol to give red crystals with m.p. 151-152°.

Anal. Calcd. for $C_{21}H_{28}O_4N_4$: C, 62.98; H, 7.05
Found: C, 62.94, H, 7.39.

Degradation of Acorenone-B

Hydrogenation of Acorenone-B (10). Preparation of Dihydroacorenone-B (25, 1-Isopropyl-4,9-dimethylspiro[4.5]dec-7-one

Acorenone-B (1.62 g) was hydrogenated for 10 hours in glacial acetic acid (40 ml) with PtO_2 (150 mg) as catalyst and with hydrogen at atomospheric pressure. The catalyst was removed by filtration using

Celite filter aid, the filtrate was diluted with 400 ml of water and extracted with ether. The ethereal solution was washed with a 5% sodium bicarbonate solution and water, dried over anhydrous $MgSO_4$ and evaporated to yield 1.5 g of oil. The infrared spectrum of the hydrogenated product showed hydroxyl absorption at 3350 cm^{-1} and carbonyl absorption at 1710 cm^{-1}. The hydrogenated product (1.4 g) was dissolved in acetone and oxidized by the dropwise addition of Jones[37] reagent* until the orange color persisted. The slight excess of Jones reagent was destroyed with isopropyl alcohol; two grams of sodium bicarbonate was added and the suspension filtered. The filtrate was dried over anhydrous $MgSO_4$ and evaporated to yield dihydroacorenone-B (25, 1.3 g, 80%). GLC analysis (flame) of 25 (3% Ucon Polar on 80/100 mesh AS column, C.T. 135°, H.F.R. 55 ml/min) showed two components R_t 10 min (23%) and R_t 11 min (77%). TLC analysis showed only one spot (R_f 0.25, benzene). Attempts to separate the two epimeric saturated ketones (25) by column chromatography on alumina and silica gel were not successful. The following physical properties of 25 were obtained using the mixture of saturated ketones: b.p. 70°/0.05 mm, $[\alpha]_D^{26°}$ + 8.8 ± 0.2° (C = 10.2, MeOH). The spectral properties of mixture 25 were: ν_{max}^{film} 1710 cm^{-1} (C=O); n.m.r. (CCl_4) 54 (6H, d, C<u>H</u>-CH_3), 59 (3H, d, CH-C<u>H</u>$_3$), 61 (3H, d, CH-C<u>H</u>$_3$) and 115, 129, 144, 158 cps (2H, doublet of doublets, O=C-CH_2-C, J = 14 cps, $\Delta_{\nu AB}$ = 27.6 cps). The mass spectrum gave the parent peak at m/e 222 (12.5%, calculated mol. wt. 222) and base peak at m/e 41.

---

*The Jones reagent was prepared by dissolving 267 g of CrO_3 in 230 ml of conc. H_2SO_4 followed by dilution to one liter with distilled water.

Anal. Calcd. for $C_{15}H_{26}O$: C, 81.02; H, 11.78.

Found: C, 80.67; H, 11.52

Found[6]: C, 81.07; H, 11.97

Preparation of the 2,4-Dinitrophenylhydrazone of Dihydroacorenone-B (25)

Dihydroacorenone-B (25, 35 mg) was added to a solution of 2,4-dinitrophenylhydrazine (42 mg) in methanol-concentrated hydrochloric acid (9:1, 2.7 ml) and heated on a steam bath for one minute. Dihydroacorenone-B 2,4-dinitrophenylhydrazone was recrystallized from ethanol to give yellow crystals with m.p. 137-138°.

ORD and CD Studies of Dihydroacorenone-B (25)

Separation of the two epimers of 25 was achieved by preparative GLC (flame) with a stream-splitter attachment. Three fractions were collected in 1/8" teflon tubes at the following GLC conditions: 0.5 µl injection, 3% Ucon-LB-550-X on 100/120 mesh Gas Chrom Q column, C.T. 135°, H.F.R. 90 ml/min., R_t 17 min (30%, 25a) R_t 18.5 min (70%, 25b). The collection of 15 injections afforded fraction 1 (1.50 mg) predominantly 25a (85% 25a, 15% 25b); fraction 2 (1.98 mg) a mixture of 25a and 25b (34% 25a, 66% 25b); and fraction 3 (4.65 mg) predominantly 25b (3% 25a, 97% 25b). The UV spectra showed: fraction 1 (85% 25a), λ_{max}^{MeOH} 278 (ε = 22); fraction 3 (97% 25b), λ_{max}^{MeOH} 283 (ε = 26). ORD of fraction 1 (85% 25a), (c, 0.252, CH_3OH), 30.5°: $[\Phi]_{450}$ + 132°; $[\Phi]_{312}$ + 825°; $[\Phi]_{287}$ ± 0°; $[\Phi]_{274}$ - 167°; $[\Phi]_{220}$ + 1,050°; a = +9.9. The ORD of fraction 1 also exhibited fine structure which appeared as shoulders at 322, 302, and 280 mµ CD of fraction 1 (85%, 25a) (C, 0.0079, CH_3OH), 32.5°: $[\Theta]_{450}$ ± 0; $[\Theta]_{295}$ + 580; $[\Theta]_{210}$ ± 0; Γ = 40 m . The CD of

fraction 1 also exhibited fine structure which appeared as shoulders at 318, 305 and 290 mμ. ORD of fraction 3 (97% 25b), (c, 0.228; CH_3OH), 34°: $[\Phi]_{589}$ + 14.6° $[\Phi]_{306}$ + 830°; $[\Phi]_{294}$ ± 0°; $[\Phi]_{272}$ - 1,390°; $[\Phi]_{230}$ - 1,530°, a = + 22.2. The ORD of fraction 3 also exhibited fine structure which appeared as shoulders at 312 and 300 mμ. ORD of fraction 3 (97% 25b), (C, 0.00105, CH_3OH), 31°: $[\Theta]_{450}$ ± 0; $[\Theta]_{292}$ + 1,510; $[\Theta]_{210}$ ± 0; Γ = 30 mμ. The CD of fraction 3 also exhibited fine structure which appeared as shoulders at 312, 303 and 285 mμ. ORD of fraction 2 (34% 25a, 66% 25b), (c, 0.0985, CH_3OH), 34.5°: $[\Phi]_{589}$ -44.7°; $[\Phi]_{308}$ + 760°; $[\Phi]_{295}$ ± 0°; $[\Phi]_{272}$ - 1,180°; $[\Phi]_{210}$ - 2,000°; a = +19.4. CD of fraction 2 (34% 25a, 66% 25b), C, 0.00447, CH_3OH), 31°: $[\Theta]_{450}$ ± 0; $[\Theta]_{293}$ + 1,250; $[\Theta]_{210}$ ± 0; Γ = 30 mμ.

Equilibrium of Dihydroacorenone (25)

The equilibration studies were carried out using fractions 1 and 3 obtained by preparative GLC of 25 as previously described. Partial equilibration occurred upon standing in methanol at room temperature for one month. GLC analysis (flame) after one month (4' x 1/4" column, 3% Ucon-LB-550X on 100/120 mesh Gas Chrom Q, C.T. programmed at 1°/min with a 16 min time delay at 110-125°, H.F.R. 95 ml/min) showed fraction 1 as a mixture of 70% 25a (R_t 31 min) and 30% 25b (R_t 34 min) and fraction 3 as a mixture of 11% 25a and 89% 25b. A standard solution of base was prepared from 43.8 mg of sodium and 100 ml of anhydrous methanol. An aliquot (0.25 ml) of the standard basic solution was added to a methanolic solution (2 ml) of 1 mg of fraction 1 (70% 25a). The solution was refluxed under nitrogen and checked intermittently by GLC analysis at the

conditions described above. After refluxing 30 min, GLC analysis showed a mixture of 29.6% 25a and 70.4% 25b which changed only slightly after six hours of reflux (31.8% 25a and 68.2% 25b). An aliquot (0.33 ml) of the standard base solution was added to a methanolic solution (3 ml) of 1.5 mg of fraction 3 (89% 25b). The solution was checked intermittently by GLC analysis at the conditions described above. After six hours of reflux, GLC analysis showed a mixture of 31.7% 25a and 68.3% 25b.

Direct Comparison of Dihydroacorenone-B (25) and Dihydroacorenone* (12)

A direct comparison of dihydroacorenone-B (25) and dihydroacorenone (12) was made by GLC analysis using the mixed injection method. The GLC (flame) conditions (3% Ucon Polar on 80/100 mesh Anakrom AS column, C.T. 126°, H.F.R. 60 ml/min) were kept constant throughout the comparison. Under these conditions dihydroacorenone-B was a mixture of two components with R_t 14.9 min (25a, 23%) and with R_t 16.3 min (25b, 77%); whereas, dihydroacorenone was a mixture of two components with R_t 13.4 min (12a, 22.5%) and R_t 15.8 min (12b, 77.5%). A series of mixed injections containing different ratios of dihydroacorenone-B and dihydroacorenone showed conclusively that dihydroacorenone-B and dihydroacorenone were two different pairs of epimeric ketones.

The mass spectrum of dihydroacorenone (12) gave the parent peak at m/e 222 (47.6%, calc. mol. wt. 222) and base peak at m/e 138. A comparison of the mass spectra of 12 and 25 showed that they both have peaks at the same m/e's but the relative intensities are quite different,

*An authentic sample of dihydroacorenone was kindly supplied by Dr. V. Herout.

e.g. different base peaks. The infrared spectrum of 12, ν_{max}^{film} 1710 cm^{-1} (C = O), was identical to the infrared spectrum of 25 except for the region 1100-1300 cm^{-1}. The n.m.r. (CCl_4) spectrum of 12 [53 (6H, d, CH-CH_3), 59 (3H, d, CH-CH_3), 62 cps (3H, d, CH-CH_3)] was very similar to the n.m.r. spectrum of 25 in the methyl region but no assignment could be made for the C-CH_2-C=O signals of dihydroacorenone (12), which appeared as a quartet in the n.m.r. spectrum of 25.

ORD of dihydroacorenone (22.5%, 12a and 77.5%, 12b), (c, 0.274, CH_3OH), 31°: $[\Phi]_{539}$ - 9.7°; $[\Phi]_{312}$ - 414°; $[\Phi]_{298}$ ± 0°; $[\Phi]_{282}$ + 471°; $[\Phi]_{220}$ + 91°; a = -8.85. CD of the same mixture (C, 0.0124, CH_3OH), 31°: $[\Theta]_{700}$ ± 0; $[\Theta]_{296}$ - 670; $[\Theta]_{220}$ 0; Γ = 27 mμ. The Cotton effect of dihydroacorenone-B (34% 25a and 66% 25b) was positive (a = +19.4) compared to a negative Cotton effect (a = -8.85) for dihydroacorenone (22.5%, 12a and 77.5%, 12b).

Hydrogenation of Acorenone-B (10): Preparation of 1-Isopropyl-4,8-dimethylspiro[4.5]dec-7-ol (26)

Acorenone-B (1.2 g) was hydrogenated for 3 days in glacial acetic acid (50 ml) with 5% Pt/C (100 mg) as the catalyst and with hydrogen at atmospheric pressure. The catalyst was removed by filtration. The filtrate was diluted with 300 ml of water and extracted with ether. The ethereal solution was washed with 5% sodium bicarbonate and water, dried over anhydrous $MgSO_4$, and evaporated to yield 1.1 g (92%) of an oil. Complete hydrogenation was determined by the absence of a carbonyl absorption band in the infrared spectrum of the oil and the presence of a strong hydroxyl band at 3300 cm^{-1}. GLC analysis (flame) of the oil

(3% Ucon Polar on 80/100 mesh Anakrom AS column, C.T. 165°, H.F.R. 80 ml/min) showed three components with R_t 2.2 min (4.1%), R_t 3.0 min (82.6%), and R_t 3.8 min (13.1%). Column chromatography of the oil (1.1 g) on alumina (40 g) afforded a pure alcohol (26) (0.6 g), b.p. 70°/0.1 mm in the benzene-ether (4:1) eluent. GLC analysis at the conditions given above showed that this alcohol (26) was the major component (R_t 3.0 min) of the hydrogenation reaction. The spectral properties of 26 were: ν_{max}^{film} 3300 cm^{-1} (O-H), 990 cm^{-1}; n.m.r. (CCl_4) 49 (3H, d, CH-CH_3, J = 6 cps), 54 (9H, d, $CHCH_3$, J = 6 cps), 226 (1H, m, H-C-OH), and 184 cps (1H, s, H-C-OH). The signal at 184 cps was reduced in intensity when D_2O was added. The mass spectrum of 26 gave the parent peak at m/e 224 (1.6%, calcd. mol. wt. 224), base peak at 163 m/e, and a peak due to elimination of water at m/e (206 40%).

Anal. Calcd. for $C_{15}H_{28}O$: C, 80.29; H, 12.57
Found: C, 80.42; H, 12.41

Oxidation of 26: Preparation of 25

An attempt was made to obtain one of the epimers of the saturated ketones by oxidizing the pure alcohol (26) obtained by chromatography on alumina. A solution of 26 (0.6 g) in acetone was titrated with the Jones reagent until the solution was light yellow. The excess reagent was destroyed with isopropyl alcohol, sodium bicarbonate (1 g) was added, and the suspension was filtered. The filtrate was dried over anhydrous $MgSO_4$ and evaporated to yield 25 (0.58 g). The infrared and n.m.r. spectra were identical with those obtained previously for 25. GLC (flame) analysis (3% Ucon Polar on 80/100 mesh Anakrom AS column, C.T. 135°, H.F.R. 55 ml/min) of the oxidation product showed it to be identical with the mixture of saturated ketones (R_t 12.4 min, 22.5%

and R_t 13.2 min, 77.5%) obtained by hydrogenation of 10.

Reduction ($LiAlH_4$) of Dihydroacorenone-B (25): Preparation of 26

Lithium aluminum hydride (250 mg) was added to anhydrous ether (50 ml). An ethereal solution of 25 (455 mg) was added dropwise to the well-stirred lithium aluminum hydride mixture. After the addition was complete, the reaction mixture was refluxed for three hours and then allowed to cool. The excess lithium aluminum hydride was destroyed by the dropwise addition of water. The ethereal solution was decanted away from the lithium salts, washed with water, dried over anhydrous $MgSO_4$, and evaporated to yield 26 (435 mg, 97%). GLC analysis (thermal) of the oil (3% PDEAS on 80/100 mesh CW column, C.T. 185°, H.F.R. 75 ml/min) showed three components with R_t 25 min (74.2%), R_t 28 min (16.1%), and R_t 31 min (9.7%). TLC analysis showed two spots (R_f 0.15 and R_f 0.09, benzene). The infrared spectrum showed strong hydroxyl absorption at 3350 cm^{-1} and absence of absorption in the carbonyl region. GLC (flame) comparison (5.0% Carbowax 20M on 90/100 mesh Anakrom AS, C.T. 200°, H.F.R. 95 ml/min) of the mixture of alcohols obtained from lithium aluminum hydride reduction of 25 with 26, obtained from the hydrogenation of 10, showed that the retention time of 26 (R_t 1.6 min) was the same as that of the major component from the lithium aluminum hydride reduction of 25.

Baeyer-Villiger Oxidation[38] of Dihydroacorenone-B (25): Preparation of 1-Isopropyl-4,9-dimethyl-8-oxaspiro[4.6]undec-7-one (27)

Dried disodium hydrogen phosphate (1.3 g) was added to a methylene chloride (25 ml) solution of 450 mg of dihydroacorenone-B (25).

Trifluoroperacetic acid was prepared by adding* trifluoroperacetic anhydride (0.76 ml) dropwise at 0° to a well stirred solution of anhydrous methylene chloride (5.0 ml) and 90 percent hydrogen peroxide (0.084 ml). The trifluoroperacetic acid solution was added slowly to the well stirred solution of 25. After complete addition, the mixture was refluxed (foaming occurred**) for one hour. The cooled solution was poured into water (50 ml) to destroy the peroxides. The presence of peroxides was determined with starch iodide paper. The methylene chloride layer was washed with water, dried over anhydrous $MgSO_4$, and evaporated to yield 400 mg (89%) of viscous oil. GLC (flame) analysis of the oil (3.8% SE-30 on 80/100 mesh CW column, C.T. 150°, H.F.R. 50 ml/min) showed one major product with R_t 11 min (73%) and two minor products with R_t 9.7 min (14%) and R_t 10.1 min (13%). The infrared spectrum of the oil showed two carbonyl absorptions at 1700 and 1725 cm^{-1}. Column chromatography of the reaction product (400 mg) on alumina gave 300 mg of a solid in the benzene-petroleum ether (b.p. 35-40°) (4:1) eluent. GLC analysis (flame) of the solid (3.8% SE-30 on 80/100 mesh CW column, C.T. 160°, H.F.R. 50 ml/min) showed two components with R_t 4.9 min (15%) and R_t 5.8 min (85%). The component corresponding to the peak with R_t 10.6 min (13%) by GLC analysis of the crude reaction product was not obtained from the column chromatography. Attempts to separate the two components by column chromatography were unsuccessful. The major

*If the trifluoroperacetic anhydride was added too rapidly the yield of the peroxy acid was lowered.

**In the cases where foaming did not appear the reaction did not go to completion.

component (R_t 5.8 min, 85%) could be obtained pure by fractional crystallization or fractional sublimation. The initial crystals which were obtained from the crystallization of the mixture from petroleum ether (b.p. 35-40°), were a mixture enriched in the minor component. The major component was obtained pure (27) from the mother liquor after two crystallizations. The first substance that sublimed at 65°/0.1 mm was a mixture enriched in the minor component; thus, major component 27 was obtained pure after repeated sublimations. The melting point (88.5-89°) of the crystals of pure 27 obtained from recrystallization or sublimation was the same. The observed spectral properties of 27 were: ν_{max}^{KBr} 1700 cm^{-1} (C=O); $\lambda_{shoulder}^{hexane}$ 218 mμ (ε = 98). CD (C, 0.0194, hexane), 34.5°: $[\Theta]_{450}$ ± 0; $[\Theta]_{225}$ + 3,030; $[\Theta]_{212}$ + 1,800; Γ = 35 mμ. ORD (c, 0.46, hexane), 32.6°: $[\Phi]_{589}$ 0°; $[\Phi]_{246}$ + 1,200°; $[\Phi]_{232}$ ± 0°; $[\Phi]_{214}$ - 4,150°. The amplitude of the positive Cotton effect could not be obtained from the ORD curve because of solvent absorption at 210 mμ. The n.m.r. (CCl_4) of 27 (Plate IV) showed signals at 52 (3H, d, $CHCH_3$, J=7 cps), 63 (6H, d, $CHCH_3$, J=6 cps), 77 (3H, d, $CHCH_3$, J=6 cps), 113, 126, 183, 196 (2H, doublet of doublets O=C-CH_2-C, J=13 cps $\Delta_{\nu AB}$ = 69 cps), and 264 cps (1H, m, O-CH-C). The mass spectrum of 27 gave the parent peak at m/e 238 (10.6%, calculated mol. wt. 238) and base peak at m/e 109.

Anal. Calcd. for $C_{15}H_{26}O_2$: C, 75.52; H, 10.99

Found: C, 75.33; H, 10.81

Reduction ($LiAlH_4$ of 27: Preparation of 1-(2-Hydroxyethyl)-2-isopropyl-5-methyl-1-cyclopentanepropanol (28)

Lithium aluminum hydride (150 mg) was added to anhydrous ether (50 ml). An ethereal solution of 27 (120 mg) was added dropwise to the

well stirred lithium aluminum hydride-ether mixture. After the addition was complete, the reaction mixture was refluxed for three hours, then allowed to cool. The excess lithium aluminum hydride was destroyed with wet ether. The ethereal solution was decanted from the lithium salts, washed with water, dried over anhydrous $MgSO_4$, and evaporated to yield 120 mg (99%) of 28 as an oil (b.p. 90°/0.1 mm). GLC (flame) analysis of 28 (3% FFAP on 80/100 mesh CW column, C.T. 220°, H.F.R. 75 ml/min) showed one peak with R_t 3.31 min. The infrared spectrum (film) of 28 showed broad hydroxyl absorption at 3350 cm^{-1} and the absence of carbonyl absorption. The n.m.r. ($CDCl_3$) spectrum of 28 showed poorly resolved methyl signals in the range of 50-80 cps, and signals at 190 (2H, s, C-OH, $W_{1/2}$ = 6 cps) and 220 cps (3H, m, CH-OH). The signal at 190 cps disappeared when D_2O was added to the sample.

Anal. Calcd. for $C_{15}H_{30}O_2$: C, 74.44; H, 12.50

Found: C, 74.24; H, 12.51

Oxidation of 28: Preparation of the Methyl Ester of 1-(3-Oxobutyl)-2-isopropyl-5-methyl-1-cyclopentaneacetic acid (29)

The diol (28, 375 mg) was added to a solution of chromium trioxide (500 mg) in glacial acetic acid (30 ml) and stirred at room temperature for two days. The solution was diluted with water (200 ml) and extracted with three 50-ml portions of ether. The ethereal extract was washed with four 25-ml portions of 5% sodium carbonate solution and with two 50-ml portions of water. The 5% sodium carbonate and water washings were combined and acidified with 1N hydrochloric acid. The acidified solution was extracted with ether. The ethereal solution was

washed with water, dried over anhydrous $MgSO_4$, and evaporated to yield 200 mg (53%) of acidic material, which was directly reacted with diazomethane in ether to give 190 mg (95%) of an oil. GLC (flame) analysis of the oil (10% SE-30 on 80/100 mesh CW column, C.T. 200°, H.F.R. 85 ml/min) showed two components with R_t 4.4 min (16%) and with R_t 8.4 min (84%). Column chromatography on alumina (25 g) gave the major component (29, R_t 8.4 min) in pure condition in the petroleum ether (b.p. 35-40°)-benzene (9:1) eluent. Evaporation of the solvent gave 120 mg (32%) of 29 as an oil (b.p. 60°/0.1 mm). The spectral properties of 29 were: ν_{max}^{film} 1720, 1730 cps; λ_{max}^{hexane} 279 mμ (ε = 53.5), λ_{max}^{hexane} 223 mμ (ε = 156). ORD of 29 (c, 0.7196, hexane), 33.5°: $[\Phi]_{589}$ + 15.3°; $[\Phi]_{304}$ - 52°; $[\Phi]_{294}$ ± 0°; $[\Phi]_{250}$ + 238°; $[\Phi]_{230}$ + 230°; a = -2.9. CD of 29 (C, 0.0268, hexane), 34°: $[\Theta]_{450}$ ± 0; $[\Theta]_{285}$ - 276; $[\Theta]_{230}$ ± 0; Γ = 50 mμ. The n.m.r. ($CDCl_3$) spectrum (Plate V) of 29 showed signals at 49 (6H, d, CH-C<u>H</u>$_3$, J = 6 cps), 55 (3H, d, CH-C<u>H</u>$_3$, J = 6 cps), 115 (3H, s, O=C-C<u>H</u>$_3$, $W_{1/2}$ = 2 cps), 132 (2H, s, C-C<u>H</u>$_2$-C=O, $W_{1/2}$ = 2.5 cps), 142 (2H, t*, CH_2-C<u>H</u>$_2$-C=O, J = 7 cps), and 198 cps (3H, s, O-C<u>H</u>$_3$, $W_{1/2}$ = 1.5 cps). The mass spectrum of 29 gave a weak parent peak at m/e 248 (1.4%, calculated mol. wt. 248) and the base peak at m/e 131.

Anal. Calcd. for $C_{16}H_{28}O_3$: C, 71.63; H, 10.52

Found: C, 72.00; H, 10.84

*The triplet was partially obscured.

Reaction* of Dihydroacorenone-B (25) with 1,2-Ethanedithiol: Preparation of the Thioketal of 25 (30)

A solution of 25 (4.0 g) in glacial acetic acid (20 ml) was added to a solution of p-toulenesulfonic acid monohydrate (1 g) in 1,2-ethanedithiol (2.13 ml). The mixture was stirred for 48 hours at room temperature, poured onto crushed ice (50 g), and extracted with three 50-ml portions of ether. The ethereal solution was washed with three 50-ml portions of a saturated solution of sodium bicarbonate and three 10-ml portions of distilled water, dried over anhydrous $MgSO_4$, and evaporated to yield 3.9 g (97%) of a yellow oil. Column chromatography of the oil (3.9 g) on alumina (140 g) gave 3.8 g of 30 (b.p. 110°/0.05 mm) in the petroleum ether (b.p. 35-40°) eluent. GLC (flame) analysis of 30 (5.0% Carbowax 20M on 90/100 mesh Anakrom AS, C.T. 200°, H.F.R. 80 ml/min) showed one major component with R_t 8.1 min (93%) and two lower boiling impurities with R_t 1.3 min (1%) and R_t 1.6 min (6%).

The n.m.r. (CCl_4) spectrum of 30 showed signals at 51 (3H, d, CH-$\underline{CH_3}$, J = 6 cps), 52 (3H, d, CH-$\underline{CH_3}$, J = 6 cps), 58 (3H, d, CH$\underline{CH_3}$, J = 7 cps), 67 (3H, d, CH-$\underline{CH_3}$, J = 7 cps); 126 (2H, s, S_2C-$\underline{CH_2}$-C, $W_{1/2}$ = 4 cps), 150-180 (1H, m, $S_2\underline{CH}$-CH_3), and 190 cps (4H, s, S-$\underline{CH_2}$-$\underline{CH_2}$-S, $W_{1/2}$ = 3 cps). The mass spectrum of 30 gave the parent and base peak at m/e 298 (100%). The precise mass determination of M_{298} using 1,2-dichlorooctafluorocyclohexene as the reference compound gave M_{298} = 298.177; the molecular weight calculated for $C_{17}H_{28}S_2$ was M_{298} 298.179.

*The preparation of 30 was done by K. Schorno[6] and the spectral data was obtained by the author.

Reduction[39] of Thioketal 30: Preparation* of 1-Isopropyl-4,8-dimethyl-spiro[4.5]undecane (31)

Lithium (1.5 g) was added to a solution of thioketal (2.69 g) in anhydrous ethylamine (100 g) which was cooled to -20°. The reaction mixture, which developed a dark blue color, was shaken at -20° for one hour. After one hour, water was added dropwise until the dark blue color was dissipated. The ethylamine was allowed to evaporate; then dry petroleum ether (b.p. 35-40°) was added and the lithium hydroxide was removed by filtration then washed with petroleum ether (b.p. 35-40°). The petroleum ether fractions were combined, dried over anhydrous $MgSO_4$, then removed by distillation through a Vigreux column at atmospheric pressure. The residue yielded 1.79 g (94%) of 31 as a clear colorless oil. GLC analysis (flame) of 31 (3% SE-30 on 80/100 mesh CW column, C.T. 140°, H.F.R. 80 ml/min) showed one main peak with R_t 2.65 min and a shoulder at 2.5 min. The 0.1 mm thick film infrared spectrum of 31 was very similar to the infrared spectrum of acorane[75]. The n.m.r. spectrum of 31 showed three signals for the protons of the four methyl groups at 48, 53, and 59 cps, the other protons showed up as a broad multiplet in the range 64-120 cps. The mass spectrum of 31 gave the present peak at m/e 208 (19%) and the base peak at m/e 124.

The precise mass determination of 31 using 1,2-dichloroctafluorocyclohexane as the reference compound gave M_{208} = 208.210; the molecular weight calculated for $C_{15}H_{28}$ was M_{208} = 208.219.

*The preparation of 31 was done by K. Schorno[6] and the spectral data was obtained by the author.

Reduction ($NaBH_4$) of Acorenone-B (10): Preparation of 1-Isopropyl-4,8-dimethylspiro[4.5]dec-7-ol (37)

A solution of sodium borohydride (120 mg) in water (2 ml) was added to a solution of 10 (100 mg) in absolute ethanol (6 ml). The solution was stirred overnight at room temperature. The solution was diluted with ether (50 ml), washed with two-25 ml portions of 1N hydrochloric acid, two 25-ml portions of 5% sodium bicarbonate, and two 25-ml portions of water. The ethereal solution was dried over anhydrous $MgSO_4$ and evaporated to give 90 mg (90%) of an oil (37). GLC (flame) analysis of 37 (10% SE-30 on 80/100 mesh CW column, C.T. 150°, H.F.R. 80 ml/min) showed two major peaks with R_t 1.7 min and R_t 1.9 min. The two peaks were not sufficiently resolved for estimation of relative areas of the peaks. The infrared spectrum of 37 showed an absence of a carbonyl absorption band and the presence of a strong hydroxyl band at 3340 cm^{-1}. The n.m.r. (CCl_4) spectrum of 37 showed a broad poorly resolved multiplet at 40-70 cps for the protons on the three methyl groups attached to saturated carbons, a broad singlet at 103 cps ($W_{1/2}$ = 7 cps) for the protons on the methyl group attached to the double bond, a multiplet at 325 cps for the olefinic proton, and multiplets at 295 cps and 200-260 cps for the hydroxyl proton and the protons on the carbon bearing the hydroxyl group.

Ozonolysis* of Acorenone-B (10): Preparation of 2-Isopropyl-5-methyl-1,1-cyclopentanediacetic acid (32)

A solution of 10 (1.4 g) in carbon tetrachloride (25 ml) was

*The procedure used was identical to the procedure used by V. Herout et al. in the ozonolysis of acorenone (3).

ozonized at 0° with a slow stream of ozone in oxygen (3%). The completion of the ozonolysis was indicated by detecting excess ozone in the exit gas by the formation of a yellow color in a potassium iodide solution. The ozonized solution was diluted with water (25 ml), stirred for ten minutes then heated at reflux temperature for one hour. The mixture was steam distilled; the non steam-volatile portion precipitated (0.8 g, 58%, m.p. 138-140°). The n.m.r. ($CDCl_3$) spectrum of the latter solid showed signals at 50-70 (poorly resolved $CH\underline{CH}_3$ protons), 142 (2H, s, O=C-$C\underline{H}_2$C, $W_{1/2}$ = 2.5 cps), 197 (2H, s, O=C-$C\underline{H}_2$, $W_{1/2}$ = 4 cps), and 637 cps (2H, s, $O\underline{H}$, $W_{1/2}$ = 7 cps). The solid was crystallized from water to give 32, m.p. 143-145° (Kofler block, uncorrected). Herout[5] et al. reported that diacid 14 obtained from acorenone melted at 145-147°. The infrared spectrum of 32 showed: ν_{max}^{KBr} 2500-2800 cm^{-1} (O=C-OH), 1700 cm^{-1} (C=O). The mass spectrum of 32 did not give a parent peak (calculated mol. wt. 242); however, it gave a peak at m/e 224 (23%) which corresponds to the loss of one mole of water to form an anhydride. Anhydride formation from diacid 32 is not unusual at the operating conditions of the mass spectrometer (analyzer 125°, 10^{-6}/mm). The mass spectrum of 32 gave the base peak at m/e 139.

Anal. Calcd. for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15

Found: C, 64.80; H, 9.02

Esterification of 32: Preparation of the Dimethyl Ester of 32 (33)

A solution of 32 (110 mg) in ether (50 ml) was esterified with an ethereal solution of diazomethane at 0°. The ethereal solution was dried over anhydrous $MgSO_4$ and evaporated to give 100 mg (91%) of an oil.

The oil was distilled (b.p. 80°/0.05 mm) to give 33 (90 mg). GLC (flame) analysis (3% FFAP on 80/100 mesh CW column, C.T. 200°, H.F.R. 70 ml/min) showed a single peak with R_t 4.2 min. The optical rotation of 33 was $[\alpha]_D^{20°}$ -7.9 ± 0.1° (C = 5.92 g/100 ml, ethanol). The infrared spectrum (Plate VI) of diester 33 showed: ν_{max}^{film} 1730 cm^{-1} (C=O). The infrared spectrum* of dimethyl ester 15 obtained by Herout[5] et al. was the same as the infrared spectrum of 33, within the limits imposed by comparing two spectra taken with different spectrophotometers. The n.m.r. ($CDCl_3$) spectrum (Plate VII) of 33 showed signals at 48 (6H, d, $CHC\underline{H}_3$, J = 6 cps), 54 (3H, d, $CHC\underline{H}_3$, J = 6 cps), 125 (2H, s, $C\text{-}C\underline{H}_2\text{-}C{=}O$, $W_{1/2}$ = 3 cps), 158 (2H, s, $C\text{-}CH_2\text{-}C{=}O$, $W_{1/2}$ = 3 cps), and 199 cps (6H, s, $O\text{-}C\underline{H}_3$, $W_{1/2}$ = 3 cps). The n.m.r. spectrum in carbon tetrachloride showed the signals at 125, 158, and 199 cps had shifted to 137, 173, and 218 cps, respectively. The mass spectrum of diester 33 did not give a parent ion (calculated mol. wt. 270); however, it gave a peak at m/e 239 (16%) which is due to the loss of an $O\text{-}CH_3$ fragment. The base peak was at m/e 153.

Anal. Calcd. for $C_{15}H_{26}O_4$: C, 66.63; H, 9.69

Found: C, 66.69; H, 9.67

Reduction ($LiAlH_4$) of 33: Preparation of 2-Isopropyl-5-methyl-1,1-cyclopentanediethanol (34)

Diester 33 (59 mg) was added to a mixture of lithium aluminum hydride (75 mg) in anhydrous ether (50 ml). The reaction mixture was refluxed for three hours, then allowed to cool. The excess lithium

*The infrared spectrum of 15 was kindly supported by Dr. V. Herout.

aluminum hydride was destroyed with wet ether. The ethereal solution was decanted from the lithium salts, washed with water, dried over anhydrous $MgSO_4$, and evaporated to yield 45 mg (75%) of solid diol 34. The solid was recrystallized from an ether-petroleum ether (b.p. 35-40°) solvent mixture to give crystals (m.p. 60-61.5°, Kofler block) of 34. The infrared spectrum (KBr) of 34 showed broad hydroxyl absorption at 3350 cm^{-1} and the absence of carbonyl absorption. GLC (flame) analysis of 34 (3% FFAP on 80/100 mesh CW column, C.T. 230°, H.F.R. 85 ml/min) showed one peak with R_t 4.3 min. The n.m.r. ($CDCl_3$) spectrum of 34 showed poorly resolved signals for the methyl protons at 50-70 cps and signals at 160 (2H, s, OH, $W_{1/2}$ = 9 cps) and 205-240 cps (4H, m, CH_2-OH. The mass spectrum of 34 gave the parent peak at m/e 214 (14%, calculated mol. wt. 214), base peak at m/e 135, and a peak at m/e 135, and a peak at m/e 178 (50%) due to the elimination of two moles of water.

Reaction of 34 with p-Toulenesulfonyl Chloride: Preparation of the Ditosylate of 34 (35)

Diol 34 (120 mg) was added to a solution of p-toulenesulfonyl-chloride (110 mg) in dry pyridine (50 ml) and stirred for twelve hours. The reaction mixture was diluted with water and extracted with three 50-ml portions of ether. The ethereal extract was washed with 1N hydrochloric acid and water, dried over anhydrous $MgSO_4$, and evaporated to yield 295 mg (98%) of solid 35. The ditosylate (35) was recrystallized from a petroleum ether (b.p. 35-40°) benzene solvent mixture to

*The triplet was partially obscured.

give 120 mg of crystalline (m.p. 78-79°, Kofler block) 35. The infrared spectrum (KBr) of 35 showed the absence of hydroxyl absorption and a band at 1605 cm^{-1} characteristic of a tosylate. The n.m.r. spectrum ($CDCl_3$) of 35 showed signals at 35-52 (9H, m, $CHC\underline{H}_3$), 101 (4H, t*, CH_2-$C\underline{H}_2$-C, J = 8 cps), 148 (3H, s, O-$C\underline{H}_3$, $W_{1/2}$ = 3 cps), 243 (2H, t, O-CH_2, J = 8 cps), 245 (2H, t, O-$C\underline{H}_2$-CH_2, J = 8 cps), and 438, 446, 465, 473 (8H, doublet of doublets, aromatic protons, J_{AB} = 8 cps, $\Delta_{\nu AB}$ = 26 cps). The two triplets at 243 and 245 cps changed to two singlets when the triplet at 101 cps was irradiated (H_1 5.0, DF -142.5 cps).

Model Reaction for the Elimination of a Primary Tosylate

Decan-1-ol (4 g) was added to a solution of p-toluenesulfonylchloride (4 g) in anhydrous pyridine and stirred for twelve hours. The reaction mixture was diluted with water and extracted with ether. The ethereal solution was washed with 1N hydrochloric acid and water, dried over anhydrous $MgSO_4$, and evaporated to yield 3.5 g of an oil. The infrared spectrum of the oil showed the absence of hydroxyl absorption and the presence of an absorption band at 1600 cm^{-1} characteristic of a tosylate. The decan-1-ol tosylate (3.5 g) was placed on a basic alumina column (70 g) in petroleum ether (b.p. 35-40°) solvent and allowed to stand on the column for twelve hours. After twelve hours the substance was eluted with petroleum ether (b.p. 35-40°) to yield 1.0 g (70%) of an oil. GLC (flame) comparison (3% SE-30 on 90/100 mesh CW column, C.T. 130°, H.F.R. 80 ml/min) of the oil with an authentic sample of 1-decene showed that the oil showed one peak with

*The triplet was partially obscured.

R_t 3.1 min and 1-decene showed one peak with the same retention time (R_t 3.1 min).

Attempted Elimination of Ditosylate 35 by Elution Through Basic Alumina

Ditosylate 35 (60 mg) was dissolved in benzene (1 ml) and placed on a basic alumina (15 g) column for 15 hours, then eluted with petroleum ether (b.p. 35-40°). Most of the ditosylate (35, 50 mg) was recovered unchanged, but GLC analysis (10% SE-30 on 80/100 mesh CW column, C.T. 150°, H.F.R. 80 ml/min) of the first 45 ml of eluent collected showed two peaks with R_t 2.1 min (90%) and R_t 3.6 min (10%); under these conditions ditosylate 35 was not eluted from the GLC column. TLC analysis of this same fraction showed one weak spot (R_f 0.89, petroleum ether). There was an insufficient amount of product to characterize further.

Studies Directed Toward the Preparation of a Crystalline Derivative Suitable for the Structure Eluciation of Acorenone-B by Single Crystal X-ray Diffraction

Attempted Preparation of Acorenone-B p-Bromophenylsulfonylhydrazide

The p-bromophenylsulfonylhydrazide used in this reaction was commercially available (Eastman Organic Chemicals) with m.p. 116° (lit.[40] m.p. 118°) and it formed an acetone derivative (m.p. 145-147, lit.[41] 145-146°) when it was mixed with an equimolar amount of acetone in methanol. Acorenone-B (10, 50 mg) was added to a solution of p-bromophenylsulfonylhydrazide (60 mg) in methanol (10 ml) at room temperature. After 12 hours no crystals had formed. A few drops of water were added to the solution, but no crystals formed. Evaporation of most of the methanol and extraction with petroleum ether (b.p. 35-40°) gave acorenone-B

(45 mg). Variations of the conditions of this reaction included adding one drop of glacial acetic acid or concentrated hydrochloric acid before or after the addition of acorenone-B (10) and heating the solution over a steam bath for one or two minutes. However, none of the desired derivative was obtained under these conditions.

Preparation of p-Iodobenzoylhydrazide

p-Iodobenzoylhydrazide was prepared as described by G. Gaudemaris and J. E. Dubois[42] except for the esterification step. A mixture of commercially available (Eastman Organic Chemicals) p-iodotoulene (40 gm), water (1.6 l), and potassium permanganate (98 gm) was refluxed for 24 hours. The manganese dioxide was removed by filtration and the filtrate was acidified with 1 N hydrochloric acid, whereupon the p-iodobenzoic acid precipitated. The precipitate was collected by filtration and dried at 110° for one hour to yield 22 g (50%) of p-iodobenzoic acid m.p. 264° (lit.[42], m.p. 265°). Diazomethane in ether solution was added to p-iodobenzoic acid (16.5 g) in ether (100 ml). The p-iodobenzoic acid was only slightly soluble in ether, so that no all of it was in solution when the diazomethane was added; however, as the ether soluble methyl ester was formed the remaining solid p-iodobenzoic acid dissolved. Methyl p-iodobenzoate (17 g, 99%) crystallized from a concentrated ether solution. The crystals melted at 115° (lit.[42] m.p. 114°). The infrared spectrum of the crystals showed ν_{max}^{KBr} 1685 cm^{-1} (C=0). Methyl p-iodobenzoate (17 g) was added to a solution of hydrazine hydrate (85%, 18 g) in absolute ethanol (10 ml) and the slurry was refluxed for twelve hours. The reaction mixture was allowed to cool and the crystalline product was filtered to yield 16 g (94%) of a solid (m.p. 163-165°). The solid material

was recrystallized twice from a methanol-water (1:1) solvent mixture to give 10 g of p-iodobenzoylhydrazide with m.p. 165° (lit.[42] m.p. 165°) and infrared spectrum: ν_{max}^{KBr} 1620 (C=O), 3175, and 3275 cm^{-1}. The n.m.r. (DMSO) spectrum of p-iodobenzoylhydrazide showed signals at 270 (2H, broad multiplet, NH-$\underline{NH}_2$, 454, 462, 468, 476 (4H, doublet of doublets, aryl protons, J_{AB} = 8 cps), 590 cps (1H, broad multiplet, $\underline{NH}$-NH_2). There was also a signal at 214 cps which may be an impurity in the solvent or some unreacted methyl p-iodobenzoate.

Attempted Preparation of Acorenone-B p-Iodobenzoylhydrazone

Acorenone-B (10, 30 mg) was added to a solution of p-iodobenzoylhydrazide (53 mg) in a methanol-water (1:1) solvent mixture. Two drops of glacial acetic acid were added to the solution. The solution was heated for two minutes on a steam bath, then allowed to cool. The only crystals obtained were those of p-iodobenzoylhydrazide. Acorenone-B was also recovered from the reaction. Acorenone-B (10) was also treated with p-iodobenzoylhydrazide in a methanol-water-hydrochloric acid (9:3:1) solvent mixture and heated for twenty minutes on a steam bath. The reaction was allowed to cool, and upon refrigeration a white precipitate formed which decomposed at 320°. Acorenone-B was recovered from the reaction mixture.

Attempted Preparation of Dihydroacorenone-B p-Iodobenzoylhydrazone

Dihydroacorenone-B (25, 35 mg) was added to a solution of p-iodobenzoylhydrazide (53 mg) in 95% ethanol (2 ml). One drop of glacial acetic acid was added and the solution was heated for 30 seconds. A white precipitate formed after 12 hours at room temperature. The preci-

cipitate (m.p. 320°) was insoluble in ether, chloroform, benzene, hexane or methanol; thus, attempts to recrystallize it failed. The infrared (nujol) spectrum showed the absence of carbonyl absorption. The solid was not further characterized.

Preparation of the Iodoacetate of 37

The iodoacetate of 37 was prepared (via the chloroacetate of 37) by a procedure used by Hodges et al.[43] for the preparation of the iodoacetate of cedrelone for X-ray analysis. The unsaturated alcohol 37 was a mixture of two alcohols obtained from the sodium borohydride reduction of acorenone-B.

The unsaturated alcohol (37, 50 mg) was added to dry benzene (10 ml) which contained dry pyridine (0.04 ml) and α-chloroacetyl anhydride (95 mg). After twelve hours at room temperature the solution was washed with 1 N hydrochloric acid, 5% sodium bicarbonate solution, and water. The benzene solution was dried over anhydrous $MgSO_4$ and evaporated to yield 55 mg (80%) of an oil. GLC (flame) analysis (10% SE-30 on 80/100 mesh CW column, C.T. 190°, H.F.R. 80 ml/min) of the oil showed two peaks (poorly resolved) with R_t 5.9 min and R_t 6.2 min which comprised approximately 70 percent of the reaction mixture. Under the same GLC conditions 37 showed two major peaks with R_t 1.8 min and R_t 1.9 min. The infrared (film) spectrum of the oil showed an absence of hydroxyl absorption and the presence of a broad carbonyl absorption at 1725 cm^{-1}. The GLC analysis and the infrared spectrum indicated that a derivative had been formed.

The derivative (55 mg) was added to a solution of sodium iodide (100 mg) in dry acetone and refluxed for 1.5 hours. The solution was

concentrated, diluted with water, and extracted with ether. The ethereal extract was dried over anhydrous $MgSO_4$ and evaporated to yield 45 mg (62%) of the crude iodoacetate of 37 as an oil. GLC (glame) analysis (10% SE-30 on 80/100 mesh CW column, C.T. 195°, H.F.R. 90 ml/min) of the oil showed two components (poorly resolved) with R_t 5.2 min and R_t 5.6 min which comprised approximately 70 percent of the reaction mixture. The infrared (film) spectrum showed a carbonyl absorption at 1727 cm^{-1}. The n.m.r. (CCl_4) spectrum of the reaction mixture indicated that the sample was impure; however, a broad signal at 220 cps ($O{=}C{-}C\underline{H}_2{-}I$) indicated that some of the desired iodoacetate was formed. Crystallization of the reaction product was not successful and no additional purification of the mixture was attempted.

Preparation of 4-Iodo-2-nitrophenylhydrazine

A solution of iodine monochloride (11.8 g) in glacial acetic acid (25 ml) was added dropwise to a well stirred solution of 2-nitroaniline* (10 g) in glacial acetic acid (700 ml) at 5-10°. After the addition was complete, the reaction mixture was allowed to warm to 20° and stirred at 20° for ten minutes. Then the solution was poured into boiling water (2 l) and boiled for two hours. Filtration of the cooled reaction mixture yielded 17 g (75%) of 4-iodo-2-nitroaniline as yellow orange crystals with m.p. 122° (lit.[44] m.p. 122°). TLC analysis of the crystals showed one spot (R_f 0.6, benzene). The n.mr. ($CD_3\overset{O}{\overset{\|}{C}}{-}CD_3$) spectrum of 4-iodo-2-nitroaniline showed signals at 426 (broad absorption, $N\underline{H}_2$), 415 (1H, d, proton at position six of benzene ring, $J_{5,6}$ = 10 cps), 455 (1H,

*Technical grade (Eastman Organic Chemicals), 2-nitroaniline (m.p. 75-77°) was used in the reaction.

doublet of doublets, proton at position five of the benzene ring, $J_{5,6}$ = 10 cps, $J_{3,5}$ = 2 cps), and 499 cps (1H, d, proton at position three of the benzene ring, $J_{3,5}$ = 2 cps). There were also signals at 127 and 184 cps which might be due to solvent impurities.

A slurry of 4-iodo-2-nitroaniline (5 g) in concentrated hydrochloric acid (20 ml) was stirred at room temperature for one hour, then cooled to 0°. A cold (0°) solution of sodium nitrite (3.5 g) in water (8 ml) was added slowly to the slurry with a dropping funnel. The tip of the dropping funnel was extended below the surface of the slurry. The reaction mixture was filtered and the filtrate was added to a cold (0°) solution of sodium hydroxide (4 g) and sodium sulfite (21 g) in water (100 ml). After stirring the mixture for 15 minutes, concentrated hydrochloric acid (30 ml) was added to the mixture slowly. The precipitate was collected by filtration, then dissolved in boiling concentrated hydrochloric acid. The hydrochloride salt of 4-iodo-2-nitrophenylhydrazine crystallized from the acidic solution after cooling to yield 2 g (35%) of yellow crystals.

The hydrochloride salt (2 g) was added to a saturated solution of sodium acetate in water and stirred for one hour. The red precipitate was collected by filtration and recrystallized from ethanol to yield 1.8 g of 4-iodo-2-nitrophenylhydrazine as red crystals with m.p. 122° (lit.[45] m.p. 123°). The infrared spectrum of 4-iodo-2-nitrophenylhydrazine showed ν_{max}^{KBr} 3090, 3340 cm^{-1} (N-H).

The 4-iodo-2-nitrophenylhydrazone derivatives of acetone and 4-methylacetophenone were prepared by mixing equimolar amounts of the carbonyl compound with the hydrazine in 95% ethanol and adding one drop of

concentrated sulfuric acid. Acetone 4-iodo-2-nitrophenylhydrazone melted at 120-121° (lit.[45] m.p. 116°) and 4-methylacetophenone 4-iodo-2-nitrophenylhydrazone melted at 178-179° (lit.[45] m.p. 172°).

Preparation of 2-Iodo-4-nitrophenylhydrazine

A solution of iodine monochloride (11.8 g) in glacial acetic acid (25 ml) was added dropwise to a well stirred solution of 4-nitroaniline* (10 g) in glacial acetic acid (700 ml) at 5-10°. After the addition was complete, the reaction mixture was allowed to warm to 20° and stirred at 20° for ten minutes. Then the solution was poured into boiling water (2 l) and boiled for two hours. Filtration of the cooled reaction mixture yielded 16 g (70%) of 2-iodo-4-nitroaniline as yellow crystals with m.p. 105° (lit.[46] m.p. 105°). TLC analysis of the crystals showed one major spot (R_f 0.5, benzene). The n.m.r. spectrum ($CD_3\overset{O}{\overset{\|}{C}}-CD_3$) of 2-iodo-4-nitroaniline showed signals at 368 (broad absorption, $\underline{NH}_2$), 418 (1H, d, proton at position six of benzene ring, $J_{5,6}$ = 9 cps) 486 (1H, doublet of doublets, proton at position five of the benzene ring, $J_{5,6}$ = 9 cps, $J_{3,5}$ = 2 cps), and 513 cps (1H, d, proton at position three of the benzene ring, $J_{3,5}$ = 2 cps). There were also signals at 127 and 184 cps which might be due to solvent impurities. The infrared spectrum (KBr) of 2-iodo-4-nitroaniline showed two aromatic amine absorption bands at 3370 and 3470 cm^{-1}.

A slurry of 2-iodo-4-nitroaniline (5 g) in concentrated hydrochloric acid (20 ml) was stirred at room temperature for one hour, then cooled to 0°. A cold (0°) solution of sodium nitrite (3.5 g) in water

*Technical grade (Eastman Organic Chemicals) 4-nitroaniline (m.p. 147°) was used in the reaction.

(8 ml) was added slowly to the slurry with a dropping funnel. The tip of the dropping funnel extended below the surface of the slurry. The reaction mixture was filtered and the filtrate was added to a cold (0°) solution of sodium hydroxide (4 g) and sodium sulfite (21 g) in water (100 ml). After stirring the mixture for 15 minutes, concentrated hydrochloric acid (30 ml) was added to the mixture slowly. The precipitate was collected by filtration, then dissolved in boiling concentrated hydrochloric acid. The hydrochloride salt of 2-iodo-4-nitrophenylhydrazine, which crystallized from the cold acid solution, was added to a saturated solution of sodium acetate in water and stirred for one hour. The dark orange precipitate was collected by filtration and recrystallized from ethanol to yield 1 g (20%) of 2-iodo-4-nitrophenylhydrazine as dark orange crystals with m.p. 148° (lit.[47] m.p. 148°).

Preparation of 5-Iodo-2-nitrophenylhydrazine

Fuming nitric acid (28 ml) was added dropwise to a slurry of 3-iodonitrobenzene (10 g) in concentrated sulfuric acid at 0°. The reaction mixture was stirred for 15 minutes after the addition was complete, then heated at 90° for two hours. The reaction solution was poured on crushed ice; the resulting yellow precipitate was collected by filtration, washed with water, and dissolved in ethanol. TLC analysis showed two spots [R_f 0.4 and R_f 0.5, benzene-petroleum ether (b.p. 35-40°) (1:5)], neither of the two spots corresponded to starting material. The component with R_f 0.5 crystallized out of the ethanol solution first to give 2 g of 4-iodo-1,2-dinitrobenzene as yellow crystals with m.p. 74° (lit.[48] m.p. 74°). A total of 0.5 g of crystalline 3-iodo-1,2-dinitrobenzene with m.p. 136° (lit.[48] m.p. 136°) was obtained from the ethanol

solution. The n.m.r. ($CD_3\overset{O}{\overset{\|}{C}}CD_3$) spectrum of 4-iodo-1,2-dinitrobenzene showed signals at 429 (1H, d, proton at position six of benzene ring, $J_{5,6}$ = 9 cps), 505 (1H, doublet of doublets, proton at position five of the benzene ring, $J_{5,6}$ = 9 cps, $J_{3,5}$ = 2 cps) 510 cps (1H, d, proton at position three of the benzene ring, $J_{3,5}$ = 2 cps).

Hydrazine hydrate (85%, 2 equivalents) was added to a slurry of 4-iodo-1,2-dinitrobenzene in ethanol (50 ml) at 0° and stirred for one hour. The resulting crystals were collected by filtration and recrystallized from ethyl acetate to yield 0.4 g of 5-iodo-2-nitrophenylhydrazine as orange red crystals with m.p. 226-227° (lit.[48] m.p. 228°). The infrared spectrum of 5-iodo-2-nitrophenylhydrazine showed ν_{max}^{KBr} 3300 and 3050 cm^{-1} (NH).

Reaction of Acorenone-B (10) with 4-Iodo-2-nitrophenylhydrazine: Preparation of Acorenone-B 4-Iodo-2-nitrophenylhydrazone (36)

Acorenone-B (10 , 38 mg) was added to a solution of 4-iodo-2-nitrophenylhydrazine (50 mg) in 95% ethanol (10 ml) containing one drop of concentrated sulfuric acid and heated for two minutes on the steam bath. Upon cooling, a red gummy solid formed. TLC analysis of the solid showed two spots (R_f 0.45 and R_f 0.60, benzene) before development in iodine vapor and a third spot (R_f 0.95) after development in iodine vapor. The spot at R_f 0.45 corresponded to the starting hydrazine and the spot at R_f 0.95 corresponded to acorenone-B. The spot at R_f 0.60 corresponded to acorenone-B 4-iodo-2-nitrophenylhydrazone (36). Column chromatography of the red gummy solid on alumina (50 g) gave 36 (40 mg) as a red glassy solid in the benzene eluent. TLC analysis of the glassy solid showed only one spot (R_f 0.6, benzene). The solid was difficult to obtain cry-

stalline; however, 36 crystallized from a supersaturated benzene-95% ethanol (3:17) solution at 43° to give bright red crystals with m.p. 89-90°. The infrared spectrum (Plate IX) of 36 showed ν_{max}^{KBr} 3310 cm^{-1} (NH) and the absence of a carbonyl absorption. The ultraviolet spectrum of 36 showed λ_{max}^{MeOH} 465 mμ (ε = 6,700), λ_{max}^{MeOH} 314 mμ (ε = 30,700), and λ_{max}^{MeOH} 266 mμ (ε = 21,100). An attempt to obtain ORD and CD curves of 36 was made, but the high absorption of light by 36 prohibited the recording of the ORD and CD curves of 36. The n.m.r. (CCl_4) spectrum (Plate VIII) of 36 showed signals at 52 (poorly resolved methyl protons), 348 (1H, m, C=C-H), 442 (2H, s, aromatic protons), 486 (1H, s, aromatic proton), and 630 cps (1H, s, N-H). The mass spectrum of 36 gave a weak parent peak at m/e 481 (1%, calculated mol. wt. 481) and the base peak at m/e 57.

Anal. Calcd. for $C_{21}H_{28}IN_3O_2$: C, 52.39; H, 5.87

Found: C, 52.21, H, 6.02

Reaction of Acorenone-B (10) with 2-Iodo-2-nitrophenylhydrazine

Acorenone-B (10), 19 mg) was added to a solution of 2-iodo-4-nitrophenylhydrazine (25 mg) in ethanol (5 ml) containing one drop of concentrated sulfuric acid and heated two minutes on a steam bath. A crystalline product was not obtained. TLC analysis showed a complex mixture. Since this reaction was not as clean as the formation of hydrazone 36, the product was not purified.

Reaction of Acorenone-B (10) with 5-Iodo-2-nitrophenylhydrazine

Acorenone-B (10 , 19 mg) was added to a solution of 5-iodo-2-nitrophenylhydrazine (25 mg) in ethanol (5 ml) containing one drop of concentrated sulfuric acid and heated on a steam bath for two minutes.

A crystalline product was not obtained. TLC analysis showed a complex mixture. Since this reaction was not as clean as the formation of hydrazone 36, the product was not purified.

X-Ray Structure Determination of Acorenone-B 4-Iodo-2-nitrophenylhydrazone (36)

Physical Description of the Crystal

Acorenone-B 4-iodo-2-nitrophenylhydrazone 36 crystallized slowly from a solvent mixture of ethanol-benzene (9:1) at 43° to form red needle crystals. Flotation in zinc nitrate solution yielded a density of 1.40 g/cc. The dimensions of the crystal used for the X-ray study were 0.913 x 0.121 x 0.063 mm (±0.002). The angles between the faces of the crystal are shown in Figure 6. The crystal was mounted along the needle axis.

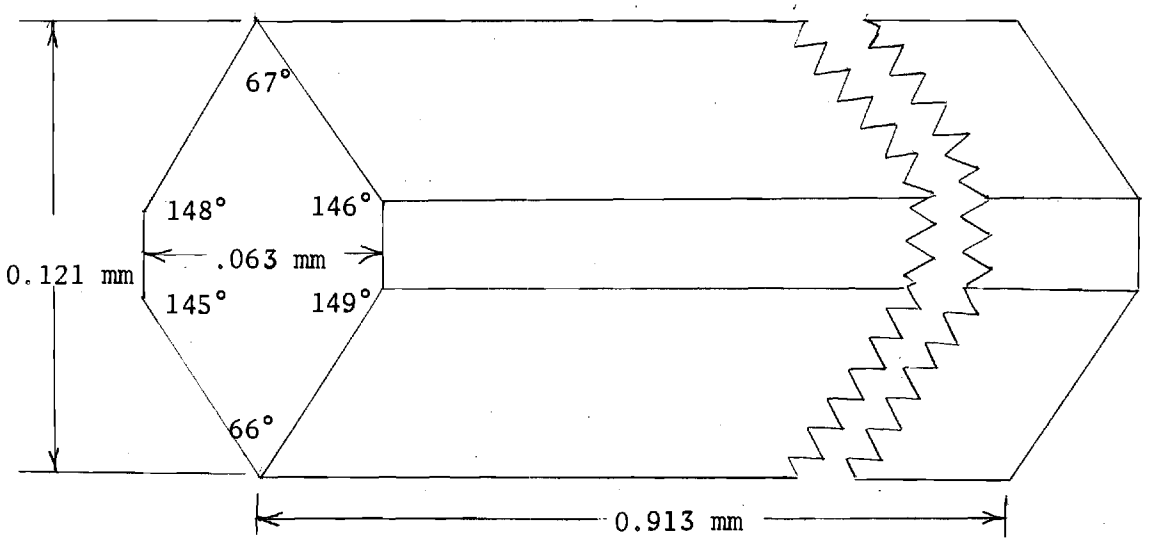


Figure 6. Shape and Dimensions of the Crystal Used for the X-ray Structure Determination.

Collection of Film Data

The film data was collected by the precession method[49] using Mo K_α (λ = 0.7093 Å) radiation. The crystal was glued on a glass fiber with fingernail polish. The glass rod was glued to a metal pin and mounted on a standard goniometer head. Orientation photographs showed zones at spindle settings of 96° 20' and 6° 20' zero and upper level photographs of both zones possessed mirror-mirror symmetry which placed the crystal in the orthorhombic system. The systematic zero level extinctions, h00, $h \neq 2n$ and 00$\underline{l}$, $\underline{l} \neq 2n$ indicated[50] the space group $P2_12_12$. This space group required at least four molecules per unit cell. The atomic coordinates of one molecule were related to the atomic coordinates of the other three molecules of the unit cell by the symmetry transformations: $\bar{x}$, $\bar{y}$, z; x, y, z; 1/2 + x, 1/2 - y, $\bar{z}$; and 1/2 - x, 1/2 + y, $\bar{z}$.

Film measurements of the reciprocal cell dimensions were a^* = 2.05 mm, b^* = 5.94 mm, and c^* = 2.88 mm. The direct cell dimension of $\underline{a}$ was obtained from a^* by the relationship $\underline{a}$ = 0.7093 Å x 60 mm/a^*. The direct cell dimensions $\underline{b}$ and $\underline{c}$ were obtained from analogous equations to give values of $\underline{a}$ = 20.81 Å (±0.01), $\underline{b}$ = 7.18 Å (±0.01), and $\underline{c}$ = 14.81 Å (±0.01). The calculated density based on four molecules of acorenone-B 4-iodo-2-nitrophenylhydrazone (mol. wt. = 481.38) and a unit cell volume of 2213 $Å^3$ was 1.44 g/cc.

Three intensity photographs of 0.5, 5, and 50 hour exposure times were recorded for each of the hkn (n = 0, 4), nk$\underline{l}$ (n = 0, 4), and hkh levels. The three photographs for each level were developed simultaneously. The intensities were estimated by visually comparing each reflection with a standard series of intensities prepared from the same cry-

stal. Only one quadrant of the film was read due to the mirror-mirror symmetry of all levels.

A total of 465 independent reflections were read and corrected for Lorentz and polarization effects.[51] The linear absorption coefficient (μ) for acorenone-B was calculated by the equation $\mu = \underline{p}\ (P_C M_C + P_O M_O + P_N M_N + P_I M_I)$ where $\underline{p}$ is the density of the crystal, P_C, P_O, P_N, and P_I are the fractions by weight of the corresponding elements and M_C, M_O, M_N, and M_I are the mass absorption coefficients of the corresponding elements for Mo K_α radiation obtained from the International Tables for X-Ray Crystallography.[52] The linear absorption coefficient so calculated was $\mu = 14.82\ cm^{-1}$. The effect of absorption on the intensity of a reflection is given by $I = I_o e^{-\mu t}$ where "t" is the thickness of the crystal through which the X-rays travel and I_o is the intensity, assuming that no absorption took place.

The evaluation of the $e^{-\mu t}$ term for the two thicknesses of the crystal used in this work yielded a transmission factor of 0.9 and 0.8 for the respective thicknesses of 0.0623 mm and 0.12 mm. The difference in the corrected intensity values was not as large as the errors in estimating the intensities, so the absorption corrections were not applied. Extinction corrections were not applied.

Structure Determination

A Patterson synthesis[53] calculated[54] from the corrected intensities showed strong iodine-iodine vectors which yielded a set of iodine coordinates which were consistent with the $P2_12_12$ space group. A structure factor calculation[55] using the iodine coordinates, x = 0.063, y = 0.234, and z = 0.188, gave an R value of 0.28. The refinement of coor-

dinates was carried out by the least-squares technique of minimizing the function E given in Equation 1, where $F_o(hk\underline{l}) = \{I_o(hk\underline{l})\}^{1/2}$ and $F_c(hk\underline{l})$

$$E = \sum_{hk\underline{l}} (|F_1(hk\underline{l})| - |F_c(hk\underline{l})|)^2 \tag{1}$$

was calculated according to Equation 2. The $F_c(hk\underline{l})$ was calculated for

$$F_c(hk\underline{l}) = \sum_{i=1}^{n} f_i e^{(-B\sin^2\theta/\lambda^2)} e[2\pi\underline{i}(hx_i + ky_i + \underline{l}z_i)] \tag{2}$$

each reflection summed over each atom "i". The f_i terms are atomic scattering factors which were obtained from International Tables for X-ray Crystallography.[52] The term $\exp(-B\sin^2\theta/\lambda^2)$ is the temperature factor which takes into account the thermal motion of the atom in the crystal. The phase relationship was calculated by the last exponential term where h, k, and $\underline{l}$ are the Miller indices and x_i, y_i, and z_i are the atomic coordinates of atom "i". The discrepancy index R was calculated by Equation 3. The correct structure was obtained by a trial-and-error

$$R = \frac{\sum_{hk\underline{l}} \left| |F_o(hk\underline{l})| - |F_c(hk\underline{l})| \right|}{\sum_{hk\underline{l}} |F_o(hk\underline{l})|} \tag{3}$$

sequence of (1) a structure-factor calculation, based on the coordinates of atoms previously located, to obtain phased $F_o(hkl)$ values; (2) an electron-density Fourier calculation,[56] using the phased $F_o(hkl)$ values, to obtain coordinates for additional atoms. The criteria used to judge the validity of the new atomic coordinates were their refinement to a

stable position and the magnitude of the temperature factor.

Several Fourier synthesis were required to locate all of the atoms. The structure factor obtained by varying all atomic coordinates and the isotropic temperature factors gave an R value of 0.109. The structure factor obtained by varying all atomic coordinates and anisotropic temperature factors of the iodine atom gave an R value of 0.087. The observed structure factors and the calculated structure factors for the 465 reflections are given in Table 1. The atomic coordinates and their estimated standard deviation and the isotropic temperature factors are given in Table 2 for the nonhydrogen atoms of acorenone-B 4-iodo-2-nitrophenylhydrazone from the refinement R 0.109. A difference Fourier did not reveal any significant peaks.

Collection of Diffractometer Data

The same crystal that was used to collect the film data was used to collect the diffractometer data. The crystal was aligned according to Picker instructions.[57] Alignment procedures revealed an apparent flaw in one face of the crystal so this face was avoided in the collection of the data. The angle settings for the Bragg reflections with positive Miller indices: h = 0-20, k = 0-6, and l = 0-14 and negative Miller indices: h = from -1 to -15, k = from -1 to -4, l = from -1 to -5, were calculated[58] and instruction cards for the diffractometer were punched out by the computer. The program used for these calculations also provided a check to insure the assignment of a right-handed coordinate system to the Miller indices of the reflections. The unit cell dimensions calculated from the angle settings of the reflections found during orientation were: $\underline{a}$ = 20.80 Å, $\underline{b}$ = 7.18 Å, $\underline{c}$ = 14.78 Å, and volume = 2208 $Å^3$.

The reflections were collected by scanning over a 2° range at a scan speed of 1°/min. The background count was taken for one minute at both ends of the scan. A standard reflection ($I_{4,2,0}$) was intermittenly scanned to check for instrument or crystal variations. No attenuation filter was used to compensate for detector counting losses and the Mo K_α radiation was unfiltered. A recorder monitored the scan of each peak. The scan of each peak was examined for erratic background and the inclusion of a peak from the K_β of Mo radiation. Reflecting positions which did not give any evidence of a peak or which included a K_β peak were discarded. A total of 1116 independent reflections were obtained in this manner.

Reduction of the Diffractometer Data

The new intensities were obtained from the expression $I = I_s - (I_{B1} + I_{B2})$ where I_s is the scan count and I_{B1} and I_{B2} are the background counts. An estimated standard deviation for a recorded number of counts was obtained from the equation $s(N) = N^{1/2}$ which is based on counting statistics. This value proved to be a low estimate as shown by the statistics of the standard reflection. The standard deviation of 77 measurements of the standard reflection was 21.7 decacounts whereas the average estimated standard deviation from counting statistics was 12.9 decacounts. The average value for the standard reflection was 1073 decacounts. Lorentz-Polarization corrections[56] were applied to the raw intensities.

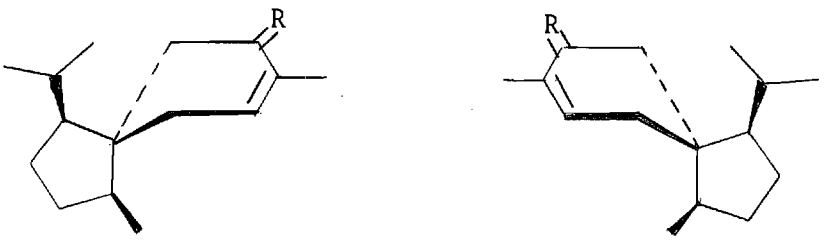
Refinement of the Diffractometer Data

The structure factor calculations were carried out with a program[59] which included the imaginary portion of the anomalous dispersion

in the calculations. The determination[60] of an absolute configuration by X-ray crystallography is based on the experimentally observable difference between I_o (hk$\underline{l}$) and $I_o(\bar{h}\bar{k}\bar{l})$ which is due to the imaginary portion of the anomalous dispersion. The only atom which significantly contributed to the anomalous dispersion was the iodine atom with a value[52] of $\Delta f'' = 2.2$ at $\sin\theta/\lambda = 0.6$. The corrections[52] for the real portion of anomalous dispersion ($\Delta f'$) for iodine were: $\Delta f' = -0.5$, $\sin\theta/\lambda = 0$; $\Delta f' = -0.7$, $\sin\theta/\lambda = 0.9$; $\Delta f' = -0.8$, $\sin\theta/\lambda = 1.3$. Values of $\Delta f'$ for intermediate $\sin\theta/\lambda$ were obtained graphically and added to the atomic scattering factors for iodine. The quantity minimized in the refinement was $\sum_{hk\underline{l}} W_{hkl} [F_o(hk\underline{l}) - F_c(hk\underline{l})]^2$ where the weighting factor was set equal to $1/s(N)$. The value of $s(N)$ is the estimated standard deviation $I_o(hk\underline{l})$ which was based on counting statistics. The weighted R value was calculated by Equation (3).

$$R_w = \frac{\sum_{hk\underline{l}} W_{hk\underline{l}} (F_o(hk\underline{l}) - F_c(hk\underline{l}))^2}{\sum_{hk\underline{l}} W_{hk\underline{l}} (F_o(hk\underline{l}))^2} \qquad (3)$$

The initial refinement of the diffractometer data was carried out with the atomic coordinates obtained from the refinement of the film data to an R value of 0.109. Two sets of coordinates were used corresponding to the two enantiomers shown in Figure 7. After three cycles of refinement varying coordinates and isotropic temperature factors, the weighted R values were 0.1223 for enantiomer A and 0.1237 for enantiomer B. The refinement after varying all atomic coordinates and the anisotropic temperature factors of iodine and C_1-C_{15} yielded $R_w = 0.0675$ for enantio-



A R = $C_6H_3IN_2O_2$ B R = $C_6H_3IN_2O_2$

Figure 7. The Two Possible Enantiomers of Acorenone-B 4-Iodo-2-nitrophenylhydrazone

mer A and R_w = 0.0702 for enantiomer B. Hamilton[61] has proposed a significance test on the R factor which has been applied to several determinations of absolute configuration[62,63]. The ratio of the R_w values for the final refinement was 1.04. An application of Hamilton's[61] significance test resulted in the assignment of A as the correct absolute configuration with a confidence level of 99.5 percent. Although this result seemed unambiguous, the separate refinement of the 774 positive hk$\underline{l}$ reflections and the negative hk$\underline{l}$ reflections did not conclusively favor either of the two possible enantiomers. Therefore, an independent check of the absolute configuration was made employing the method of Bijvoet[60,64] which involves the comparison of the F_o(hk$\underline{l}$) and F_c(hk$\underline{l}$) values for pairs of hk$\underline{l}$ and $\bar{h}\bar{k}\bar{\underline{l}}$ reflections. A comparison of the sign of the quantity (F_o(hk$\underline{l}$) - F_o($\bar{h}\bar{k}\bar{\underline{l}}$)) with ($F_c$(hk$\underline{l}$) - ($F_2\bar{h}\bar{k}\bar{\underline{l}}$)) was made with the atomic coordinates of A and B which gave R_w = 0.0697 and R_w = 0.0722

respectively. Bijvoet pairs with a difference in F_c's of less than four percent of F_o were disregarded. The atomic coorcinates of A yielded 65 Bijvoet pairs in agreement with the absolute configuration and 28 pairs in disagreement (see Table 3). The atomic coordinates of B gave 60 Bijvoet pairs in disagreement with the absolute configuration and 31 pairs in agreement (see Table 4). A total of 323 Bijovet pairs were compared. The method of comparing Bijvoet pairs significantly favors the enantiomer A supporting the conclusion reached through Hamilton's R factor significance test.

The final refinement of the structure with the diffractometer data was accomplished by varying the atomic coordinates of all the atoms and on the next cycle varying the anisotropic temperature factors of all the atoms. The refinement was stopped when the coordinates and temperature factors did not change more than fifty percent of their estimated standard deviations. The weighted R value was 0.057 for the final refinement; Table 5 contains the observed and calculated structure factors and their estimated standard deviation based upon counting statistics. A difference Fourier did not show any peaks of the intensity expected for carbon atoms. However, numerous peaks of the intensity expected for hydrogen atoms were observed, but there were more peaks than the total number of hydrogen atoms possible and a complete set of hydrogen atoms was not located.

Table 6 lists the x, y, and z coordinates for each atom. The estimated standard deviation is given in parenthesis beside the number and corresponds to the uncertainty in the last significant digit. Anisotropic temperature factors are given in Table 7 with the estimated standard

Table 1. Observed and Calculated Structure Factors from the Film Data.

H	K	L	FO	FC	H	K	L	FO	FC	H	K	L	FO	FC	H	K	L	FO	FC	H	K	L	FO	FC
6	0	0	239	229	14	1	1	22	19	6	3	2	56	61	14	0	4	48	19	0	1	7	27	17
8	0	0	113	113	15	1	1	33	26	7	3	2	47	41	0	1	4	48	43	1	1	7	34	30
10	0	0	113	113	17	1	1	43	37	8	3	2	42	50	1	1	4	66	62	2	1	7	50	46
14	0	0	64	60	19	1	1	26	23	9	3	2	35	44	3	1	4	161	142	3	1	7	43	45
16	0	0	51	47	0	2	1	32	24	10	3	2	25	28	4	1	4	29	22	4	1	7	86	89
20	0	0	44	29	1	2	1	121	130	11	3	2	37	35	7	1	4	26	24	7	1	7	23	21
22	0	0	37	24	2	2	1	71	68	12	3	2	26	27	8	1	4	26	24	0	2	7	58	66
1	1	0	36	31	3	2	1	79	78	13	3	2	27	27	9	1	4	85	84	1	2	7	68	68
2	1	0	40	45	4	2	1	82	81	0	4	2	39	50	10	1	4	32	27	2	2	7	22	25
4	1	0	234	221	5	2	1	38	42	2	4	2	25	38	11	1	4	78	67	3	2	7	24	22
6	1	0	105	108	6	2	1	43	52	3	4	2	44	52	16	1	4	31	15	4	2	7	31	34
7	1	0	31	35	7	2	1	111	121	4	4	2	36	50	1	2	4	74	72	7	2	7	24	31
8	1	0	53	55	8	2	1	27	27	7	4	2	38	42	2	2	4	19	25	0	3	7	31	35
9	1	0	35	40	9	2	1	34	35	9	4	2	27	28	3	2	4	28	19	1	3	7	40	44
10	1	0	101	94	10	2	1	54	60	10	4	2	28	32	4	2	4	43	38	2	3	7	34	37
11	1	0	27	28	12	2	1	31	26	0	5	2	24	27	5	2	4	63	59	3	3	7	37	40
12	1	0	49	41	13	2	1	45	41	1	5	2	26	40	6	2	4	31	30	7	3	7	34	30
15	1	0	22	24	15	2	1	34	31	7	5	2	29	33	7	2	4	77	71	1	4	7	36	35
16	1	0	40	32	0	3	1	78	84	0	0	3	142	137	9	2	4	41	22	2	4	7	27	30
18	1	0	34	30	1	3	1	27	22	1	0	3	154	147	10	2	4	51	52	3	4	7	29	24
0	2	0	183	196	2	3	1	28	38	2	0	3	62	67	12	2	4	28	22	4	4	7	27	30
1	2	0	138	132	3	3	1	79	92	6	0	3	103	105	14	2	4	30	9	0	0	8	126	123
2	2	0	262	260	4	3	1	28	34	7	0	3	62	60	0	3	4	71	82	1	0	8	20	21
3	2	0	189	181	5	3	1	35	47	8	0	3	84	79	1	3	4	48	54	2	0	8	47	45
4	2	0	69	72	6	3	1	46	49	9	0	3	29	26	2	3	4	45	51	3	0	8	32	38
5	2	0	95	102	8	3	1	37	39	12	0	3	42	37	3	3	4	48	60	4	0	8	21	21
6	2	0	60	62	9	3	1	38	42	13	0	3	45	37	5	3	4	52	48	8	0	8	56	52
8	2	0	143	141	11	3	1	32	34	14	0	3	54	36	6	3	4	55	66	1	1	8	21	21
10	2	0	56	48	12	3	1	23	28	15	0	3	40	24	8	3	4	53	49	2	1	8	48	54
11	2	0	45	45	14	3	1	35	31	16	0	3	41	29	9	3	4	27	26	3	1	8	23	24
13	2	0	37	44	1	4	1	39	44	1	1	3	89	77	11	3	4	42	45	4	1	8	65	65
14	2	0	45	46	2	4	1	56	53	2	1	3	131	127	13	3	4	31	7	8	1	8	25	21
16	2	0	33	19	3	4	1	22	12	3	1	3	80	80	1	4	4	34	33	0	2	8	61	61
17	2	0	24	14	4	4	1	56	69	5	1	3	68	80	2	4	4	36	42	1	2	8	31	41
19	2	0	25	25	5	4	1	32	36	6	1	3	21	15	4	4	4	36	39	2	2	8	40	42
20	2	0	26	23	6	4	1	33	34	7	1	3	31	26	10	4	4	46	36	3	2	8	50	50
1	3	0	65	69	7	4	1	23	23	8	1	3	44	47	0	5	4	35	42	8	2	8	51	57
2	3	0	53	64	8	4	1	24	23	9	1	3	48	48	2	5	4	28	36	1	3	8	34	31
4	3	0	57	65	9	4	1	24	22	10	1	3	72	73	0	0	5	171	161	2	3	8	25	30
5	3	0	43	41	10	4	1	34	33	11	1	3	34	41	1	0	5	59	58	4	3	8	26	37
6	3	0	56	51	12	4	1	25	27	12	1	3	56	53	2	0	5	80	78	1	4	8	26	33
7	3	0	70	77	0	5	1	24	35	16	1	3	29	28	3	0	5	17	19	2	4	8	27	29
9	3	0	36	35	2	5	1	25	38	17	1	3	31	16	4	0	5	64	56	3	4	8	30	32
10	3	0	30	33	6	5	1	36	34	18	1	3	32	16	5	0	5	44	51	0	0	9	21	22
12	3	0	31	31	0	0	2	107	95	0	2	3	97	112	1	1	5	34	31	1	0	9	82	72
13	3	0	32	35	1	0	2	91	97	1	2	3	47	51	2	1	5	98	91	9	0	9	38	29
15	3	0	24	19	5	0	2	96	107	2	2	3	67	72	3	1	5	18	22	1	1	9	38	37
16	3	0	24	23	6	0	2	93	88	3	2	3	55	52	4	1	5	127	132	2	1	9	23	22
0	4	0	52	56	7	0	2	80	79	4	2	3	38	33	5	1	5	19	19	3	1	9	66	67
1	4	0	43	49	8	0	2	80	80	5	2	3	68	60	0	2	5	118	113	9	1	9	46	42
2	4	0	35	25	9	0	2	42	40	6	2	3	69	69	1	2	5	51	52	1	2	9	47	44
3	4	0	106	122	12	0	2	64	47	7	2	3	47	55	2	2	5	45	48	2	2	9	34	39
4	4	0	43	41	13	0	2	41	33	8	2	3	64	65	3	2	5	79	80	3	2	9	26	26
5	4	0	87	96	14	0	2	42	37	9	2	3	47	58	4	2	5	38	41	4	2	9	24	26
6	4	0	31	33	15	0	2	44	36	10	2	3	25	16	5	2	5	35	45	9	2	9	38	30
7	4	0	31	27	0	1	2	21	27	11	2	3	26	17	1	3	5	49	54	0	3	9	41	42
8	4	0	39	41	1	1	2	76	77	12	2	3	38	33	2	3	5	51	51	1	3	9	25	16
9	4	0	32	35	2	1	2	133	126	13	2	3	28	20	3	3	5	24	29	2	3	9	26	19
11	4	0	40	52	3	1	2	104	107	14	2	3	41	35	4	3	5	51	51	3	3	9	28	27
13	4	0	24	22	4	1	2	153	145	15	2	3	30	33	5	3	5	21	27	2	4	9	28	27
1	5	0	40	47	5	1	2	86	84	0	3	3	60	60	1	4	5	35	34	4	4	9	29	32
7	5	0	34	36	6	1	2	60	51	1	3	3	60	64	3	4	5	49	62	0	0	10	45	47
3	6	0	35	43	7	1	2	35	35	2	3	3	31	37	5	4	5	31	45	2	0	10	48	46
5	6	0	43	48	8	1	2	42	39	3	3	3	52	61	1	5	5	38	38	1	1	10	23	15
0	1	1	52	51	9	1	2	49	46	4	3	3	67	69	0	0	6	24	26	2	1	10	42	35
3	0	1	180	181	10	1	2	78	67	5	3	3	41	56	1	0	6	93	99	4	1	10	49	43
4	0	1	70	70	11	1	2	62	61	6	3	3	49	50	2	0	6	40	40	10	1	10	40	33
5	0	1	119	115	12	1	2	46	45	7	3	3	25	27	4	0	6	61	50	0	2	10	57	55
6	0	1	13	11	13	1	2	34	28	8	3	3	37	33	0	1	6	40	40	2	2	10	25	21
7	0	1	151	135	16	1	2	38	30	9	3	3	47	54	1	1	6	69	68	1	3	10	26	25
8	0	1	28	19	17	1	2	28	17	10	3	3	39	41	2	1	6	65	57	4	3	10	28	25
9	0	1	85	88	0	2	2	47	57	12	3	3	29	27	3	1	6	75	82	0	0	11	33	36
10	0	1	41	41	1	2	2	73	78	13	3	3	30	26	4	1	6	69	58	1	0	11	55	57
11	0	1	33	35	2	2	2	102	101	2	4	3	80	46	6	1	6	37	22	1	1	11	24	22
12	0	1	40	38	13	2	2	25	29	3	4	3	38	37	0	2	6	58	51	2	1	11	25	29
13	0	1	52	51	4	2	2	65	68	4	4	3	36	46	1	2	6	70	73	3	1	11	39	34
14	0	1	31	24	5	2	2	78	80	5	4	3	40	46	2	2	6	51	55	4	1	11	37	35
15	0	1	39	38	6	2	2	43	41	8	4	3	30	37	3	2	6	22	17	11	1	11	29	22
16	0	1	23	3	7	2	2	76	81	9	4	3	30	34	4	2	6	59	55	1	2	11	36	37
19	0	1	26	18	8	2	2	52	59	10	4	3	31	33	0	3	6	57	57	2	2	11	26	32
21	0	1	27	13	9	2	2	44	42	11	4	3	31	28	1	3	6	22	23	0	3	11	25	16
1	1	1	155	143	10	2	2	23	20	0	5	3	24	28	2	3	6	23	36	1	3	11	26	29
2	1	1	27	21	11	2	2	41	40	1	5	3	37	42	3	3	6	36	47	3	3	11	30	24
3	1	1	149	145	12	2	2	42	31	4	5	3	29	18	4	3	6	24	33	0	0	12	24	21
4	1	1	45	45	14	2	2	37	30	1	0	4	100	100	6	3	6	39	38	0	1	12	35	26
5	1	1	74	79	15	2	2	38	28	3	0	4	32	34	0	4	6	23	22	1	1	12	36	20
6	1	1	56	54	16	2	2	28	22	4	0	4	13	2	2	4	6	37	44	2	1	12	27	28
8	1	1	17	19	0	3	2	62	65	7	0	4	34	78	4	4	6	38	41	3	1	12	29	20
9	1	1	67	59	1	3	2	55	64	8	0	4	17	16	0	0	7	69	68	4	1	12	27	29
10	1	1	42	41	2	3	2	43	53	9	0	4	86	86	1	0	7	85	78	0	0	13	51	51
11	1	1	79	77	3	3	2	43	54	10	0	4	22	8	2	0	7	55	53	0	2	13	37	28
12	1	1	29	28	4	3	2	58	70	11	0	4	24	28	3	0	7	51	41	4	1	13	29	24
13	1	1	30	26	5	3	2	39	43	12	0	4	25	10	7	0	7	47	41					

Table 2. Atomic Coordinates and Isotropic Temperature Factors Obtained from the Film Data.

Atom	x	y	z	B
C1	0.371(4)*	0.19(1)	0.259(7)	8(3)
C2	0.346(3)	0.13(1)	0.349(6)	4(2)
C3	0.281(2)	0.035(7)	0.361(4)	0.1(1)
C4	0.246(3)	0.036(9)	0.282(5)	3(2)
C5	0.269(3)	0.116(8)	0.180(5)	2(2)
C6	0.324(3)	0.27(1)	0.207(6)	5(2)
C7	0.358(4)	0.33(1)	0.100(5)	6(2)
C8	0.318(6)	0.47(2)	0.066(9)	12(4)
C9	0.270(6)	0.54(2)	0.147(9)	12(4)
C10	0.298(4)	0.46(1)	0.220(6)	6(2)
C11	0.255(3)	-0.056(8)	0.443(4)	2(1)
C12	0.241(4)	0.49(1)	0.286(6)	5(2)
C13	0.362(4)	0.15(1)	0.037(6)	6(2)
C14	0.407(8)	0.00(2)	0.08(1)	20(6)
C15	0.407(6)	0.19(2)	-0.041(8)	14(4)
N1	0.376(3)	0.128(8)	0.425(6)	6(2)
N2	0.437(3)	0.196(8)	0.426(4)	3(1)
N3	0.567(3)	0.304(8)	0.438(4)	4(1)
O1	0.620(3)	0.397(7)	0.453(4)	7(2)
O2	0.548(3)	0.320(9)	0.361(4)	8(2)
C21	0.528(3)	0.278(9)	0.670(5)	5(2)
C22	0.568(3)	0.348(8)	0.595(4)	2(1)
C23	0.531(3)	0.264(9)	0.522(4)	2(2)
C24	0.468(4)	0.22(1)	0.502(6)	5(2)
C25	0.436(4)	0.18(1)	0.592(6)	6(2)
C26	0.454(3)	0.19(1)	0.680(6)	5(2)
IODINE	0.571(3)	0.2905(9)	0.8037(5)	7.4(0.2)

*Numbers in parentheses here and in succeeding tables are estimated standard deviations in the least significant digits.

Table 3. Comparison of the Sign of the Quantities [F_o (h, k, $\underline{1}$) - F_o ($\bar{h}$,$\bar{k}$,$\bar{\underline{1}}$)] and [F_c(h,k,$\underline{1}$) - F_c($\bar{h}$,$\bar{k}$,$\bar{\underline{1}}$)] Obtained from the Refinement of the Atomic Coordinates of A

H	K	L	FO	FC
5	1	1	+	+
8	1	1	+	+
2	2	1	+	+
3	2	1	+	+
8	2	1	+	+
12	2	1	+	+
13	2	1	-	-
1	3	1	+	+
5	3	1	-	-
7	3	1	-	+
1	4	1	+	+
2	4	1	-	+
3	4	1	+	+
4	4	1	+	+
5	4	1	-	-
7	4	1	-	-
8	4	1	-	+
9	4	1	+	-
10	4	1	-	+
6	2	2	+	-
4	2	2	-	-
10	2	2	-	-
13	2	2	-	+
4	3	2	+	+
2	4	2	-	-
4	4	2	-	-
5	4	2	+	+
6	4	2	+	-
6	1	3	+	+
7	1	3	-	-
13	1	3	-	-
3	2	3	-	-
7	2	3	-	-
2	3	3	+	-
5	3	3	-	-
7	3	3	+	+
11	3	3	-	-
1	4	3	+	-
2	4	3	+	-
3	4	3	+	+
12	4	3	+	+
4	1	4	+	+
8	1	4	-	-
14	1	4	-	-
6	2	4	+	+
8	2	4	+	-
9	2	4	-	-
12	2	4	+	+
14	2	4	+	-
13	3	4	+	+
6	4	4	+	+
5	4	4	+	+
3	1	5	+	-
5	1	5	+	+
6	1	5	+	+
7	1	5	-	+
8	1	5	-	+
2	2	5	-	-
1	3	5	-	-
5	3	5	+	+
6	3	5	+	-
8	3	5	-	-
12	3	5	+	-
2	4	5	-	-
6	4	5	+	+
5	1	6	-	-
6	1	6	-	+
8	1	6	+	+
4	2	6	-	-
8	2	6	+	+
9	2	6	+	+
11	2	6	-	-
12	2	6	+	-
1	3	6	+	+
10	3	6	+	-
7	4	6	+	+
11	2	7	-	-
10	2	7	+	+
2	2	7	-	+
3	2	7	-	-
4	2	7	-	+
5	2	7	+	-
7	2	7	-	-
8	2	7	+	+
12	2	7	+	-
10	3	7	-	+
11	3	7	+	-
1	4	7	-	-
2	4	7	-	+
3	4	7	+	-
6	4	7	+	+

Table 4. Comparison of the Sign of the Quantities [(F_o(h,k,$\underline{1}$) - F_o ($\bar{h}$,$\bar{k}$,$\bar{\underline{1}}$)] and [F_c(h,k,$\underline{1}$) - F_c($\bar{h}$,$\bar{k}$,$\bar{\underline{1}}$)] Obtained from the Refinement of the Atomic Coordinates of B.

H	K	L	FO	FC
5	1	1	+	-
8	1	1	+	-
2	2	1	+	-
3	2	1	+	-
8	2	1	+	-
12	2	1	+	-
13	2	1	-	+
1	3	1	+	-
5	3	1	-	+
7	3	1	-	-
1	4	1	+	-
2	4	1	-	-
3	4	1	+	-
4	4	1	+	-
5	4	1	-	+
7	4	1	-	+
9	4	1	+	+
8	4	1	-	-
10	4	1	-	-
3	2	2	-	+
4	2	2	-	+
6	2	2	+	+
10	2	2	-	+
13	2	2	-	-
4	3	2	+	-
2	4	2	-	+
4	4	2	-	+
6	4	2	+	+
6	1	3	+	-
7	1	3	-	+
13	1	3	-	+
3	2	3	+	-
7	2	3	-	+
2	3	3	+	+
5	3	3	-	+
7	3	3	+	-
11	3	3	-	+
1	4	3	+	+
2	4	3	+	+
3	4	3	+	-
4	1	4	+	-
8	1	4	-	+
14	1	4	-	+
5	2	4	+	-
6	2	4	+	-
8	2	4	+	+
9	2	4	-	+
12	2	4	+	-
14	2	4	+	+
13	3	4	+	-
5	4	4	+	-
6	4	4	+	-
3	1	5	+	+
6	1	5	+	-
7	1	5	-	-
8	1	5	-	+
1	3	5	-	+
2	3	5	-	+
5	3	5	+	-
6	3	5	+	+
8	3	5	-	+
12	3	5	+	+
2	4	5	-	+
6	4	5	+	-
5	1	6	-	+
6	1	6	-	-
8	1	6	+	-
4	2	6	-	+
8	2	6	+	-
9	2	6	+	-
11	2	6	-	+
12	2	6	+	+
1	3	6	+	-
10	3	6	+	+
7	4	6	+	-
2	2	7	-	-
3	2	7	-	+
4	2	7	-	-
5	2	7	+	+
7	2	7	-	+
8	2	7	+	-
10	2	7	+	-
11	2	7	-	+
12	2	7	+	+
10	3	7	-	-
11	3	7	+	+
1	4	7	-	+
2	4	7	-	-
3	4	7	+	+
6	4	7	+	-

Table 5. Observed and Calculated Structure Factors Obtained from the Diffractometer Data.

H	K	L	FO	FC	SIG
8	0	0	116	111	.58
10	0	0	116	111	.57
14	0	0	64	61	.70
16	0	0	51	54	.77
20	0	0	40	42	.90
6	1	0	109	110	.37
8	1	0	50	50	.45
10	1	0	94	99	.46
12	1	0	53	56	.53
15	1	0	22	22	.86
16	1	0	38	36	.69
18	1	0	37	38	.76
1	2	0	118	118	.35
3	2	0	155	158	.36
4	2	0	62	61	.39
5	2	0	86	89	.39
6	2	0	55	56	.43
8	2	0	125	127	.44
10	2	0	52	54	.51
11	2	0	43	45	.57
13	2	0	38	38	.65
14	2	0	44	44	.64
16	2	0	26	23	.82
17	2	0	27	21	.83
19	2	0	27	24	.89
20	2	0	30	26	.88
1	3	0	57	57	.45
2	3	0	50	51	.45
4	3	0	53	56	.54
5	3	0	40	42	.62
6	3	0	48	47	.53
7	3	0	57	62	.53
8	3	0	23	15	.81
9	3	0	30	29	.67
10	3	0	31	32	.62
12	3	0	30	30	.97
13	3	0	32	27	.68
15	3	0	25	25	.86
16	3	0	25	21	.87
0	4	0	53	57	.52
1	4	0	41	38	.59
2	4	0	29	29	.62
3	4	0	94	98	.50
4	4	0	41	40	.62
5	4	0	79	79	.52
6	4	0	24	16	.75
7	4	0	27	25	.73
8	4	0	35	35	.67
9	4	0	29	22	.76
11	4	0	36	38	.68
13	4	0	29	20	.75
17	4	0	29	23	.87
1	5	0	35	28	.66
7	5	0	30	23	.74
9	5	0	23	14	.84
13	5	0	24	19	.89
3	6	0	33	29	.73
5	6	0	39	38	.72
6	0	1	12	3	.77
7	0	1	148	140	.38
8	0	1	31	25	.52
9	0	1	94	87	.43
10	0	1	46	42	.49
11	0	1	39	35	.54
12	0	1	52	45	.53
13	0	1	62	65	.54
14	0	1	32	27	.75
15	0	1	48	45	.62
19	0	1	28	24	.84
5	1	1	79	76	.36
6	1	1	59	56	.39
7	1	1	19	18	.56
8	1	1	21	20	.58
9	1	1	69	67	.44
10	1	1	48	47	.50
11	1	1	84	84	.48
12	1	1	35	32	.60
13	1	1	33	34	.63
14	1	1	26	21	.72
15	1	1	30	25	.71
16	1	1	17	12	1.18
17	1	1	47	43	.66
19	1	1	32	31	.80
0	2	1	38	36	.41
1	2	1	124	122	.36
2	2	1	70	70	.37
3	2	1	80	79	.38
4	2	1	80	80	.38
5	2	1	37	38	.44
6	2	1	46	46	.44
7	2	1	106	107	.42
8	2	1	27	25	.58
9	2	1	43	43	.51
10	2	1	57	59	.50
11	2	1	19	20	.77
12	2	1	31	29	.65
13	2	1	45	44	.59
14	2	1	14	19	1.27
15	2	1	34	30	.70
16	2	1	21	23	.94
0	3	1	70	74	.43
1	3	1	26	25	.52
2	3	1	27	26	.52
3	3	1	71	71	.44
4	3	1	29	29	.52
6	3	1	45	44	.50
7	3	1	18	11	.70
8	3	1	37	39	.54
9	3	1	37	35	.56
10	3	1	22	16	.71
11	3	1	33	29	.64
12	3	1	24	23	.75
13	3	1	20	14	.86
14	3	1	34	30	.69
16	3	1	23	16	.85
17	3	1	25	24	.87
1	4	1	34	36	.54
2	4	1	44	41	.53
3	4	1	23	20	.66
4	4	1	55	56	.52
5	4	1	28	31	.63
6	4	1	32	30	.60
7	4	1	21	18	.70
8	4	1	21	14	.73
9	4	1	21	19	.82
10	4	1	30	28	.70
12	4	1	25	22	.77
16	4	1	22	16	.93
0	5	1	25	17	.72
1	5	1	19	17	.83
2	5	1	25	22	.70
6	5	1	26	26	.74
7	5	1	18	12	.92
8	5	1	22	15	.83
2	6	1	24	18	.81
7	0	2	82	77	.40
8	0	2	88	84	.42
9	0	2	49	47	.46
10	0	2	13	12	.94
11	0	2	17	14	.78
12	0	2	60	58	.52
13	0	2	42	43	.60
14	0	2	47	49	.61
15	0	2	49	49	.61
16	0	2	19	14	.97
17	0	2	20	23	.95
6	1	2	60	57	.40
7	1	2	38	36	.45
8	1	2	42	42	.46
9	1	2	55	53	.46
10	1	2	77	78	.47
11	1	2	61	61	.50
12	1	2	49	48	.55
13	1	2	33	32	.62
16	1	2	35	35	.70
0	2	2	45	48	.41
1	2	2	66	63	.38
2	2	2	89	94	.38
3	2	2	18	14	.57
4	2	2	55	55	.41
5	2	2	70	72	.41
6	2	2	38	42	.49
7	2	2	67	68	.44
8	2	2	48	48	.49
9	2	2	40	44	.52
10	2	2	23	20	.67
11	2	2	38	35	.58
12	2	2	36	37	.60
13	2	2	28	28	.69
14	2	2	31	31	.70
15	2	2	33	36	.72
16	2	2	25	22	.82
20	2	2	22	17	.98
0	3	2	60	59	.44
1	3	2	55	52	.45
2	3	2	40	40	.47
3	3	2	42	41	.47
4	3	2	50	51	.47
5	3	2	36	36	.52
6	3	2	54	53	.49
7	3	2	40	44	.53
8	3	2	38	39	.56
9	3	2	32	35	.60
10	3	2	25	22	.69
11	3	2	33	32	.64
12	3	2	22	24	.80
13	3	2	27	27	.75
14	3	2	21	16	.85
15	3	2	21	18	.90
16	3	2	21	14	.92
0	4	2	38	36	.55
2	4	2	24	24	.65
3	4	2	31	33	.59
4	4	2	30	32	.61
5	4	2	14	10	.88
6	4	2	18	15	.81
7	4	2	28	28	.65
8	4	2	15	9	.96
9	4	2	24	22	.75
10	4	2	24	23	.78
12	4	2	21	18	.85
13	4	2	21	16	.84
0	5	2	22	19	.81
1	5	2	26	24	.72
2	5	2	20	15	.79
3	5	2	15	7	.91
4	5	2	15	11	.96
5	5	2	16	10	.94
6	5	2	19	13	.88
7	5	2	27	24	.74
8	5	2	18	14	.94
5	0	3	77	75	.38
6	0	3	121	116	.39
7	0	3	68	64	.41
8	0	3	96	93	.42
9	0	3	30	24	.76
10	0	3	16	14	.79
11	0	3	14	9	.95
12	0	3	45	45	.65
13	0	3	44	41	.59
14	0	3	54	53	.59
15	0	3	33	31	.72
16	0	3	41	45	.68
17	0	3	18	13	1.04
18	0	3	15	8	1.36
20	0	3	33	29	.85
4	1	3	122	119	.37
5	1	3	75	72	.39
6	1	3	26	24	.51
7	1	3	32	30	.48
8	1	3	48	46	.46
9	1	3	51	48	.48
10	1	3	72	72	.48
11	1	3	36	37	.58
12	1	3	60	61	.53
13	1	3	23	18	.75
15	1	3	19	17	.92
16	1	3	35	33	.71
17	1	3	28	29	.81
18	1	3	30	29	.81
19	1	3	20	14	.99
0	2	3	98	99	.39
1	2	3	46	44	.43
3	2	3	48	50	.42
4	2	3	35	37	.46
5	2	3	59	62	.43
6	2	3	62	64	.44
7	2	3	43	44	.48
8	2	3	62	66	.48
9	2	3	43	46	.53
10	2	3	20	19	.72
11	2	3	26	26	.67
12	2	3	36	37	.61
13	2	3	29	28	.70
14	2	3	39	41	.65
15	2	3	24	24	.83
16	2	3	23	19	.87
17	2	3	22	24	.94
0	3	3	54	52	.47
1	3	3	59	57	.46
2	3	3	27	29	.55
3	3	3	44	48	.58
4	3	3	54	55	.47
5	3	3	38	41	.51
6	3	3	40	39	.57
7	3	3	28	29	.59
8	3	3	27	29	.61
9	3	3	40	40	.60
10	3	3	30	30	.64
11	3	3	18	14	.87
12	3	3	27	26	.77
13	3	3	27	26	.75
14	3	3	23	19	.83
15	3	3	23	25	.91
16	3	3	21	15	.95
0	4	3	16	12	.96
1	4	3	18	18	.79
2	4	3	22	25	.69
3	4	3	33	32	.59

Table 5. (Continued).

H	K	L	FO	FC	SIG
4	4	3	28	30	.63
5	4	3	35	35	.58
7	4	3	23	23	.73
8	4	3	28	27	.69
9	4	3	26	22	.73
10	4	3	25	23	.78
11	4	3	25	26	.80
12	4	3	22	15	.83
7	5	3	28	24	.73
0	5	3	23	18	.81
1	5	3	27	25	.74
3	6	3	20	19	.91
1	0	4	104	102	.35
3	0	4	44	38	.40
4	0	4	14	15	.73
5	0	4	86	80	.40
6	0	4	14	3	.75
7	0	4	116	110	.42
8	0	4	19	18	1.32
9	0	4	84	84	.46
10	0	4	29	29	.63
11	0	4	29	27	.63
13	0	4	64	65	.56
15	0	4	49	48	.63
18	0	4	26	22	.89
0	1	4	49	45	.41
1	1	4	63	63	.39
3	1	4	137	132	.37
4	1	4	30	28	.47
5	1	4	120	117	.40
6	1	4	43	40	.46
7	1	4	32	32	.50
8	1	4	29	28	.55
9	1	4	79	76	.47
10	1	4	29	31	.61
11	1	4	76	77	.51
12	1	4	21	19	.81
13	1	4	33	32	.65
14	1	4	23	22	.81
16	1	4	24	21	.84
17	1	4	30	26	.78
19	1	4	26	21	.88
0	2	4	12	11	.94
1	2	4	67	67	.42
2	2	4	21	20	.63
3	2	4	28	30	.50
4	2	4	37	40	.49
5	2	4	56	57	.45
6	2	4	27	28	.57
7	2	4	68	70	.47
8	2	4	16	16	.89
9	2	4	36	35	.58
10	2	4	50	53	.55
12	2	4	22	23	.80
13	2	4	39	39	.64
14	2	4	14	16	1.13
15	2	4	33	32	.72
16	2	4	22	21	.90
0	3	4	60	58	.47
1	3	4	50	46	.49
2	3	4	44	43	.51
3	3	4	44	46	.50
5	3	4	49	51	.51
6	3	4	47	47	.52
8	3	4	42	45	.56
9	3	4	29	28	.65
11	3	4	41	42	.63
13	3	4	18	16	.95
14	3	4	28	23	.77
0	4	4	19	20	.93
1	4	4	31	27	.63
2	4	4	34	30	.63
4	4	4	31	31	.69
5	4	4	24	21	.70
6	4	4	14	7	.95
7	4	4	22	20	.75
8	4	4	16	12	1.04
10	4	4	26	28	.78
0	5	4	28	23	.77
2	5	4	26	23	.78
3	5	4	21	19	.79
6	5	4	23	18	.81
8	5	4	25	20	.81
1	0	5	64	62	.39
2	0	5	81	81	.39
3	0	5	15	15	.64
4	0	5	63	57	.42
5	0	5	50	47	.46
6	0	5	134	127	.42
7	0	5	11	6	1.01
8	0	5	143	139	.45
12	0	5	51	52	.58
14	0	5	76	78	.58
15	0	5	33	38	.78
16	0	5	47	47	.73
17	0	5	25	27	.91
20	0	5	26	21	.98
1	1	5	33	31	.52
2	1	5	101	94	.40
3	1	5	25	22	.59
4	1	5	138	134	.41
5	1	5	17	20	.72
6	1	5	42	42	.49
7	1	5	36	34	.52
8	1	5	43	39	.52
9	1	5	27	26	.63
10	1	5	72	72	.51
11	1	5	24	27	.73
12	1	5	56	55	.57
14	1	5	21	16	.91
15	1	5	18	12	1.02
16	1	5	32	30	.77
18	1	5	28	25	.84
0	2	5	108	105	.43
1	2	5	53	49	.47
2	2	5	47	48	.48
3	2	5	81	77	.45
4	2	5	39	39	.49
5	2	5	37	41	.51
6	2	5	101	106	.46
7	2	5	22	21	.69
8	2	5	80	80	.49
9	2	5	34	34	.60
10	2	5	23	24	.73
11	2	5	43	47	.60
12	2	5	47	47	.61
13	2	5	27	28	.78
14	2	5	48	53	.66
15	2	5	21	18	.92
16	2	5	33	36	.78
17	2	5	19	21	1.10
18	2	5	20	17	1.04
19	2	5	22	17	.99
1	3	5	46	45	.53
2	3	5	48	48	.53
3	3	5	23	24	.71
4	3	5	45	47	.53
5	3	5	23	24	.68
6	3	5	23	22	.71
7	3	5	42	45	.57
8	3	5	24	23	.71
9	3	5	28	29	.69
12	3	5	33	33	.72
13	3	5	20	17	.95
15	3	5	21	15	.92
1	4	5	31	28	.66
2	4	5	23	22	.78
3	4	5	47	44	.60
4	4	5	19	18	.83
5	4	5	37	37	.61
6	4	5	18	14	.85
8	4	5	26	31	.77
9	4	5	32	34	.72
13	4	5	22	20	.91
1	5	5	31	26	.73
5	5	5	20	10	.92
7	5	5	25	18	.81
1	6	5	20	5	.98
2	6	5	22	14	.92
3	6	5	25	15	.91
1	0	6	99	100	.41
2	0	6	46	47	.46
3	0	6	18	20	.64
4	0	6	63	58	.45
5	0	6	146	136	.43
7	0	6	88	86	.47
8	0	6	43	43	.54
9	0	6	36	36	.60
10	0	6	28	28	.69
11	0	6	23	21	.74
13	0	6	57	55	.60
15	0	6	60	66	.65
16	0	6	19	16	1.15
17	0	6	23	18	1.18
19	0	6	24	23	1.06
0	1	6	46	45	.48
1	1	6	63	62	.45
2	1	6	63	57	.46
3	1	6	77	73	.45
4	1	6	69	67	.45
5	1	6	72	68	.46
6	1	6	34	32	.54
8	1	6	16	9	.83
9	1	6	66	66	.52
10	1	6	27	25	.67
11	1	6	64	65	.55
12	1	6	29	29	.72
13	1	6	20	17	.89
14	1	6	26	29	.82
15	1	6	24	19	.88
17	1	6	29	24	.85
18	1	6	24	23	.96
19	1	6	23	18	1.04
0	2	6	60	57	.49
1	2	6	65	64	.48
2	2	6	56	55	.51
3	2	6	21	19	.79
4	2	6	55	59	.50
5	2	6	59	60	.50
7	2	6	70	73	.51
8	2	6	36	39	.60
9	2	6	21	19	.77
10	2	6	38	39	.61
11	2	6	18	16	.89
12	2	6	19	16	.88
13	2	6	42	45	.66
14	2	6	19	15	1.01
15	2	6	39	40	.72
18	2	6	25	24	.92
0	3	6	55	56	.54
1	3	6	24	19	.75
2	3	6	30	27	.66
3	3	6	34	32	.65
4	3	6	28	30	.63
5	3	6	24	22	.69
6	3	6	36	36	.61
7	3	6	25	25	.71
8	3	6	29	27	.66
9	3	6	27	30	.73
10	3	6	18	14	.89
11	3	6	28	30	.76
12	3	6	28	28	.77
14	3	6	26	20	.84
0	4	6	24	23	.81
2	4	6	38	40	.66
3	4	6	20	13	.90
4	4	6	35	35	.64
5	4	6	17	18	.91
6	4	6	14	12	1.05
7	4	6	17	18	.91
8	4	6	22	22	.83
10	4	6	30	32	.77
3	5	6	14	4	1.26
6	5	6	21	20	.92
8	5	6	23	13	.86
2	6	6	22	13	.98
1	0	7	84	90	.44
2	0	7	50	50	.47
3	0	7	51	48	.47
5	0	7	26	24	.63
8	0	7	75	74	.51
9	0	7	43	45	.58
12	0	7	23	22	.82
16	0	7	21	24	1.04
0	1	7	27	26	.68
1	1	7	37	36	.56
2	1	7	53	51	.51
3	1	7	51	50	.51
4	1	7	88	85	.48
5	1	7	63	62	.49
6	1	7	23	21	.66
7	1	7	29	22	.62
8	1	7	30	26	.63
9	1	7	40	39	.59
10	1	7	41	39	.60
11	1	7	44	47	.61
12	1	7	30	27	.71
15	1	7	21	17	.95
16	1	7	26	20	.89
17	1	7	23	23	.98
19	1	7	19	18	1.21
0	2	7	54	54	.53
1	2	7	64	65	.51
2	2	7	26	25	.74
3	2	7	31	34	.66
4	2	7	34	32	.63
5	2	7	29	32	.63
6	2	7	40	42	.57
7	2	7	30	32	.63
8	2	7	18	16	.82
9	2	7	25	26	.73
10	2	7	24	21	.77
11	2	7	23	22	.79
12	2	7	24	22	.81
0	3	7	34	35	.69
1	3	7	38	35	.64
2	3	7	31	32	.71
3	3	7	33	31	.68
4	3	7	22	22	.86

Table 5. (Continued).

H	K	L	FO	FC	SIG
5	3	7	33	32	.62
6	3	7	29	29	.67
7	3	7	30	28	.68
8	3	7	25	21	.74
9	3	7	22	15	.82
10	3	7	21	15	.81
11	3	7	21	17	.87
12	3	7	24	25	.85
13	3	7	20	13	.94
14	3	7	21	15	.94
0	4	7	25	22	.84
1	4	7	27	26	.80
2	4	7	25	17	.84
3	4	7	20	20	.96
4	4	7	24	22	.88
5	4	7	17	15	.94
6	4	7	19	18	.87
0	0	8	110	118	.51
2	0	8	47	48	.51
3	0	8	28	27	.60
4	0	8	25	24	.66
5	0	8	29	29	.63
6	0	8	83	83	.51
8	0	8	58	56	.59
10	0	8	17	20	.98
11	0	8	18	7	.94
12	0	8	32	29	.76
14	0	8	37	40	.74
16	0	8	40	41	.77
19	0	8	24	19	1.06
20	0	8	27	16	1.06
1	1	8	27	22	.67
2	1	8	53	53	.53
3	1	8	23	17	.77
4	1	8	67	67	.52
5	1	8	20	15	.77
6	1	8	23	21	.71
7	1	8	10	13	1.34
8	1	8	31	26	.65
9	1	8	38	37	.62
10	1	8	47	46	.60
11	1	8	27	23	.75
12	1	8	38	37	.68
15	1	8	28	30	.85
16	1	8	29	26	.85
17	1	8	21	10	1.06
18	1	8	27	24	.92
0	2	8	63	62	.54
1	2	8	34	33	.67
2	2	8	39	37	.62
3	2	8	49	47	.59
4	2	8	20	17	.89
5	2	8	21	21	.75
6	2	8	42	42	.59
7	2	8	20	17	.80
8	2	8	48	51	.60
9	2	8	23	22	.79
11	2	8	22	19	.83
12	2	8	22	18	.85
13	2	8	25	19	.82
14	2	8	32	33	.79
19	2	8	23	16	1.04
1	3	8	29	29	.77
2	3	8	25	18	.82
4	3	8	33	31	.73
5	3	8	23	21	.77
6	3	8	20	13	.83
7	3	8	26	26	.74
8	3	8	19	18	.89
9	3	8	21	16	.87
10	3	8	20	18	.89
12	3	8	25	23	.84
1	4	8	24	22	.91
2	4	8	23	16	.95
3	4	8	25	19	.88
5	4	8	27	28	.77
1	0	9	74	77	.51
3	0	9	16	15	.98
4	0	9	16	15	.96
5	0	9	40	42	.59
7	0	9	63	66	.57
9	0	9	40	37	.74
13	0	9	39	43	.73
15	0	9	33	33	.82
0	1	9	22	19	.83
1	1	9	37	39	.65
2	1	9	20	20	.90
3	1	9	71	73	.54
5	1	9	63	64	.56
6	1	9	28	24	.71
8	1	9	23	27	.79
9	1	9	42	39	.65
11	1	9	41	42	.67
13	1	9	22	20	.91
17	1	9	25	22	.97
19	1	9	25	18	.98
1	2	9	49	46	.60
2	2	9	35	34	.70
3	2	9	25	24	.85
4	2	9	26	28	.83
5	2	9	37	38	.71
7	2	9	38	38	.65
9	2	9	29	28	.76
10	2	9	25	22	.82
12	2	9	23	21	.87
13	2	9	23	25	.90
15	2	9	28	26	.86
0	3	9	34	34	.81
1	3	9	20	20	1.01
2	3	9	21	18	.99
3	3	9	31	28	.84
5	3	9	26	24	.87
6	3	9	30	33	.79
8	3	9	23	24	.83
9	3	9	19	18	.98
1	4	9	14	7	1.44
2	4	9	22	23	1.04
3	4	9	13	7	1.54
4	4	9	28	23	.88
7	4	9	19	16	.96
10	4	9	22	20	.95
0	5	9	21	9	1.11
2	5	9	19	14	1.19
1	0	10	30	26	.68
2	0	10	41	47	.60
6	0	10	41	44	.62
8	0	10	52	53	.63
7	0	10	20	18	.91
9	0	10	20	20	.94
12	0	10	31	30	.83
14	0	10	30	27	.86
15	0	10	21	17	1.08
0	1	10	17	13	1.08
1	1	10	19	16	1.02
2	1	10	41	39	.65
3	1	10	16	7	1.12
5	1	10	24	22	.88
6	1	10	19	13	1.02
8	1	10	22	23	.87
10	1	10	38	35	.74
12	1	10	26	24	.85
0	2	10	53	57	.63
1	2	10	12	16	1.48
2	2	10	22	20	.94
3	2	10	21	21	.98
5	2	10	33	33	.78
6	2	10	31	27	.80
7	2	10	15	12	1.10
8	2	10	32	30	.74
9	2	10	24	29	.84
11	2	10	22	17	.89
12	2	10	22	17	.93
14	2	10	21	20	1.05
4	3	10	29	26	.88
3	3	10	19	15	1.11
1	3	10	26	24	.93
2	3	10	20	11	1.07
5	3	10	18	16	1.20
9	3	10	20	14	.97
0	4	10	21	19	1.11
3	4	10	23	19	1.05
4	4	10	18	7	1.24
5	4	10	27	23	.96
1	0	11	50	55	.61
3	0	11	16	16	1.01
5	0	11	31	33	.72
6	0	11	24	25	.83
7	0	11	47	48	.67
9	0	11	20	15	1.01
10	0	11	23	19	.95
1	1	11	25	26	.93
2	1	11	29	29	.83
3	1	11	37	37	.73
4	1	11	41	44	.69
5	1	11	27	27	.86
6	1	11	21	28	1.05
8	1	11	16	16	1.12
9	1	11	26	24	.84
10	1	11	25	20	.90
0	2	11	20	20	1.12
1	2	11	33	34	.79
2	2	11	31	30	.84
3	2	11	21	20	1.06
4	2	11	26	23	.95
5	2	11	29	24	.87
6	2	11	21	11	1.05
7	2	11	30	28	.77
8	2	11	23	20	.87
9	2	11	21	16	.94
10	2	11	19	15	1.03
0	3	11	23	15	1.05
1	3	11	24	23	1.01
3	3	11	24	18	1.02
4	3	11	16	18	1.42
6	3	11	26	25	.99
2	4	11	23	20	1.08
4	4	11	26	18	1.02
10	4	11	22	13	.98
0	0	12	23	25	1.30
3	0	12	15	11	1.19
4	0	12	18	13	.99
5	0	12	17	10	1.01
6	0	12	22	17	.91
7	0	12	29	30	.79
0	1	12	28	25	.87
1	1	12	31	29	.81
2	1	12	26	22	.89
4	1	12	31	31	.84
7	2	12	24	19	1.01
4	1	13	32	30	.85
10	1	13	25	26	.95
0	2	13	33	34	.87
1	0	14	30	35	.86
7	0	14	29	29	.87
-4	-1	-1	43	48	.40
-5	-1	-1	84	82	.36
-6	-1	-1	57	57	.39
-7	-1	-1	16	18	.62
-8	-1	-1	22	22	.56
-9	-1	-1	62	67	.45
-10	-1	-1	42	46	.51
-11	-1	-1	75	85	.49
-12	-1	-1	27	33	.72
-1	-2	-1	127	126	.36
-2	-2	-1	76	76	.37
-3	-2	-1	85	83	.38
-4	-2	-1	77	82	.39
-5	-2	-1	36	39	.45
-6	-2	-1	43	45	.45
-7	-2	-1	100	105	.43
-8	-2	-1	30	29	.55
-9	-2	-1	40	43	.51
-10	-2	-1	54	61	.51
-11	-2	-1	19	20	.79
-12	-2	-1	31	31	.63
-13	-2	-1	38	41	.65
-15	-2	-1	23	30	.89
-1	-3	-1	27	27	.51
-2	-3	-1	25	26	.54
-3	-3	-1	67	71	.44
-4	-3	-1	30	30	.51
-5	-3	-1	32	34	.54
-6	-3	-1	44	44	.50
-7	-3	-1	18	13	.74
-8	-3	-1	35	40	.57
-9	-3	-1	36	36	.58
-10	-3	-1	20	16	.74
-11	-3	-1	30	29	.65
-12	-3	-1	22	23	.79
-14	-3	-1	30	29	.74
-1	-4	-1	39	37	.54
-2	-4	-1	42	42	.54
-3	-4	-1	25	22	.66
-4	-4	-1	60	59	.52
-5	-4	-1	28	29	.66
-6	-4	-1	30	30	.61
-7	-4	-1	20	17	.78
-8	-4	-1	19	15	.79
-9	-4	-1	21	17	.80
-10	-4	-1	29	29	.71
-12	-4	-1	23	23	.82
-3	-1	-2	106	110	.34
-4	-1	-2	137	136	.34
-5	-1	-2	97	95	.37
-6	-1	-2	56	56	.40
-7	-1	-2	34	35	.46
-8	-1	-2	40	42	.47
-9	-1	-2	50	53	.47
-10	-1	-2	70	77	.47
-11	-1	-2	55	61	.52
-12	-1	-2	43	48	.57
-13	-1	-2	28	32	.67
-1	-2	-2	62	63	.38
-2	-2	-2	88	91	.38
-3	-2	-2	15	8	.60
-4	-2	-2	53	52	.41
-5	-2	-2	70	73	.41
-6	-2	-2	38	38	.49
-7	-2	-2	66	68	.44

Table 5. (Continued).

H	K	L	FO	FC	SIG
-8	-2	-2	47	50	.49
-9	-2	-2	39	43	.52
-10	-2	-2	21	19	.72
-11	-2	-2	37	35	.58
-12	-2	-2	34	37	.62
-13	-2	-2	27	29	.71
-14	-2	-2	29	32	.72
-15	-2	-2	31	36	.72
-1	-3	-2	52	54	.45
-2	-3	-2	39	39	.47
-3	-3	-2	40	40	.48
-4	-3	-2	54	54	.47
-5	-3	-2	37	36	.51
-6	-3	-2	54	53	.49
-7	-3	-2	40	43	.54
-8	-3	-2	36	38	.57
-9	-3	-2	32	35	.60
-10	-3	-2	23	22	.71
-11	-3	-2	32	33	.66
-12	-3	-2	25	25	.74
-13	-3	-2	26	26	.77
-14	-3	-2	20	15	.89
-15	-3	-2	20	19	.91
-2	-4	-2	22	23	.71
-3	-4	-2	32	33	.59
-4	-4	-2	29	30	.63
-5	-4	-2	17	13	.80
-6	-4	-2	19	14	.77
-7	-4	-2	28	28	.66
-9	-4	-2	27	23	.70
-10	-4	-2	24	22	.81
-12	-4	-2	22	18	.85
-13	-4	-2	19	16	.94
-1	-1	-3	84	82	.34
-2	-1	-3	127	123	.34
-3	-1	-3	78	79	.36
-4	-1	-3	119	119	.36
-5	-1	-3	71	72	.39
-6	-1	-3	27	26	.49
-7	-1	-3	29	29	.49
-8	-1	-3	45	46	.46
-9	-1	-3	45	47	.49
-10	-1	-3	67	72	.48
-11	-1	-3	33	38	.59
-12	-1	-3	54	60	.54
-13	-1	-3	19	17	.85
-14	-1	-3	13	9	1.10
-15	-1	-3	20	17	.89
-1	-2	-3	44	44	.41
-2	-2	-3	64	69	.40
-3	-2	-3	52	53	.41
-4	-2	-3	35	36	.45
-5	-2	-3	60	63	.43
-6	-2	-3	62	65	.44
-7	-2	-3	43	41	.48
-8	-2	-3	60	65	.48
-9	-2	-3	44	47	.52
-10	-2	-3	21	19	.72
-11	-2	-3	26	26	.67
-12	-2	-3	34	37	.63
-13	-2	-3	27	28	.73
-14	-2	-3	35	39	.67
-15	-2	-3	24	25	.83
-1	-3	-3	55	58	.46
-2	-3	-3	28	28	.54
-3	-3	-3	43	47	.58
-4	-3	-3	53	56	.48
-5	-3	-3	36	39	.54
-6	-3	-3	41	40	.56
-7	-3	-3	30	32	.60
-8	-3	-3	25	30	.67
-9	-3	-3	39	40	.60
-10	-3	-3	27	30	.69
-11	-3	-3	18	14	.87
-12	-3	-3	28	26	.76
-13	-3	-3	27	26	.77
-14	-3	-3	22	19	.89
-15	-3	-3	26	24	.84
-1	-4	-3	19	16	.74
-2	-4	-3	25	24	.65
-3	-4	-3	36	34	.57
-4	-4	-3	30	31	.62
-5	-4	-3	37	36	.59
-6	-4	-3	19	11	.77
-7	-4	-3	25	23	.70
-8	-4	-3	27	26	.70
-9	-4	-3	29	21	.69
-10	-4	-3	25	23	.78
-11	-4	-3	26	25	.79
-12	-4	-3	23	16	.83
-13	-4	-3	19	16	.93
-14	-4	-3	15	6	1.13
-1	-1	-4	59	62	.38
-2	-1	-4	9	10	.86
-3	-1	-4	132	134	.37
-4	-1	-4	32	30	.45
-5	-1	-4	113	116	.40
-6	-1	-4	40	39	.46
-7	-1	-4	29	31	.51
-8	-1	-4	28	27	.54
-9	-1	-4	73	77	.47
-10	-1	-4	28	32	.62
-11	-1	-4	69	78	.52
-12	-1	-4	21	19	.79
-13	-1	-4	31	33	.67
-14	-1	-4	21	21	.84
-1	-2	-4	62	65	.41
-2	-2	-4	20	20	.59
-3	-2	-4	29	31	.49
-4	-2	-4	36	39	.50
-6	-2	-4	29	30	.57
-7	-2	-4	68	72	.47
-8	-2	-4	16	14	.84
-9	-2	-4	35	33	.57
-10	-2	-4	48	52	.54
-11	-2	-4	13	7	1.03
-12	-2	-4	22	23	.78
-13	-2	-4	38	39	.64
-14	-2	-4	14	15	1.11
-15	-2	-4	32	31	.74
-1	-3	-4	47	47	.48
-2	-3	-4	41	45	.50
-3	-3	-4	45	45	.50
-5	-3	-4	48	51	.51
-6	-3	-4	46	47	.53
-8	-3	-4	41	44	.57
-9	-3	-4	28	27	.67
-11	-3	-4	40	43	.62
-12	-3	-4	18	10	.94
-13	-3	-4	18	17	.93
-14	-3	-4	27	23	.78
-1	-4	-4	31	28	.59
-2	-4	-4	33	29	.59
-4	-4	-4	32	31	.68
-5	-4	-4	26	22	.68
-6	-4	-4	17	9	.85
-7	-4	-4	22	20	.78
-8	-4	-4	16	12	1.05
-10	-4	-4	28	28	.77
-12	-4	-4	20	14	.98
-15	-4	-4	22	17	.92
-1	-1	-5	32	32	.46
-2	-1	-5	93	93	.40
-3	-1	-5	25	20	.53
-4	-1	-5	131	133	.41
-5	-1	-5	21	21	.61
-6	-1	-5	43	45	.48
-7	-1	-5	35	35	.52
-8	-1	-5	41	42	.52
-9	-1	-5	25	26	.65
-10	-1	-5	67	70	.51
-11	-1	-5	22	27	.78
-12	-1	-5	51	56	.57
-14	-1	-5	18	16	.94
-15	-2	-5	23	18	.89
-1	-2	-5	48	50	.45
-2	-2	-5	43	44	.46
-3	-2	-5	73	78	.44
-4	-2	-5	39	41	.49
-5	-2	-5	38	41	.51
-6	-2	-5	97	103	.46
-7	-2	-5	20	22	.73
-8	-2	-5	77	80	.50
-9	-2	-5	34	35	.60
-10	-2	-5	24	24	.70
-11	-2	-5	42	46	.60
-12	-2	-5	42	47	.64
-13	-2	-5	27	28	.79
-14	-2	-5	48	55	.64
-1	-3	-5	43	44	.51
-3	-3	-5	22	23	.67
-4	-3	-5	47	48	.52
-5	-3	-5	25	24	.66
-6	-3	-5	23	21	.69
-7	-3	-5	44	45	.56
-8	-3	-5	24	22	.73
-9	-3	-5	30	30	.66
-10	-3	-5	25	24	.73
-12	-3	-5	33	32	.70
-13	-3	-5	19	17	.97
-15	-3	-5	17	15	1.07
-1	-4	-5	27	29	.67
-2	-4	-5	19	21	.81
-3	-4	-5	43	45	.59
-5	-4	-5	36	37	.63
-6	-4	-5	22	15	.75
-7	-4	-5	16	9	.93
-8	-4	-5	28	31	.73
-9	-4	-5	33	33	.70
-11	-4	-5	39	43	.71
-12	-4	-5	22	18	.91
-13	-4	-5	22	21	.90
-14	-4	-5	22	15	.92
-1	-1	-6	57	62	.44
-2	-1	-6	59	58	.44
-3	-1	-6	68	75	.44
-4	-1	-6	67	68	.45
-5	-1	-6	65	65	.46
-6	-1	-6	32	33	.54
-8	-1	-6	16	10	.83
-9	-1	-6	60	65	.52
-10	-1	-6	23	24	.73
-11	-1	-6	56	64	.56
-12	-1	-6	25	28	.77
-13	-1	-6	20	18	.85
-1	-2	-6	59	63	.46
-2	-2	-6	51	55	.48
-3	-2	-6	22	19	.62
-4	-2	-6	54	57	.49
-5	-2	-6	57	60	.49
-6	-2	-6	15	12	.89
-7	-2	-6	68	74	.51
-8	-2	-6	36	40	.60
-9	-2	-6	23	22	.73
-10	-2	-6	37	39	.62
-11	-2	-6	17	16	.90
-12	-2	-6	20	15	.86
-13	-2	-6	37	44	.68
-11	-3	-6	29	30	.72
-10	-3	-6	19	13	.87
-12	-3	-6	26	27	.80
-1	-3	-6	25	21	.63
-2	-3	-6	28	28	.61
-3	-3	-6	33	32	.58
-4	-3	-6	29	31	.62
-5	-3	-6	24	22	.69
-6	-3	-6	37	35	.61
-7	-3	-6	27	26	.68
-8	-3	-6	28	27	.68
-9	-3	-6	29	29	.71
-2	-4	-6	35	39	.65
-4	-4	-6	35	35	.64
-7	-4	-6	20	19	.85
-8	-4	-6	23	23	.82
-9	-4	-6	21	13	.85
-10	-4	-6	32	32	.74
-12	-4	-6	26	23	.83
-13	-4	-6	21	16	.96
-1	-1	-7	33	35	.53
-2	-1	-7	49	50	.48
-3	-1	-7	47	50	.49
-4	-1	-7	78	86	.47
-5	-1	-7	59	62	.49
-6	-1	-7	21	21	.69
-7	-1	-7	25	21	.66
-8	-1	-7	27	26	.68
-9	-1	-7	35	39	.62
-10	-1	-7	37	39	.61
-11	-1	-7	40	47	.62
-12	-1	-7	31	27	.68
-1	-2	-7	59	64	.50
-2	-2	-7	25	27	.64
-3	-2	-7	30	31	.58
-4	-2	-7	32	34	.58
-5	-2	-7	30	31	.60
-6	-2	-7	40	43	.56
-7	-2	-7	28	30	.65
-8	-2	-7	19	18	.83
-9	-2	-7	25	25	.71
-10	-2	-7	24	23	.75
-11	-2	-7	20	21	.85
-12	-2	-7	24	20	.78
-1	-3	-7	35	35	.59
-2	-3	-7	30	30	.63
-3	-3	-7	29	31	.64
-4	-3	-7	23	21	.73
-5	-3	-7	32	33	.63
-6	-3	-7	30	30	.66
-7	-3	-7	28	28	.70
-8	-3	-7	23	20	.79
-9	-3	-7	21	15	.81
-10	-3	-7	19	16	.90
-11	-3	-7	21	16	.86
-12	-3	-7	24	25	.85
-1	-4	-7	27	25	.72
-2	-4	-7	22	18	.78
-3	-4	-7	21	18	.81
-4	-4	-7	26	21	.73
-5	-4	-7	18	15	.92
-6	-4	-7	20	19	.84

Table 6. Atomic Coordinates Obtained from the Diffractometer Data.

Atom	x	y	z
C1	-0.3749(8)	0.199(3)	0.269(1)
C2	-0.3437(8)	0.124(3)	0.355(1)
C3	-0.2807(9)	0.045(3)	0.355(2)
C4	-0.245(1)	0.032(3)	0.274(2)
C5	-0.267(1)	0.124(3)	0.181(2)
C6	-0.3237(9)	0.266(2)	0.201(1)
C7	-0.359(1)	0.325(4)	0.106(2)
C8	-0.312(2)	0.464(5)	0.057(3)
C9	-0.264(2)	0.553(4)	0.131(2)
C10	-0.301(1)	0.466(3)	0.229(1)
C11	-0.2552(9)	-0.054(3)	0.441(2)
C12	-0.243(1)	0.478(3)	0.301(2)
C13	-0.365(1)	0.159(5)	0.034(2)
C14	-0.407(2)	-0.003(6)	0.080(3)
C15	-0.390(2)	0.265(7)	-0.053(2)
N1	-0.375(8)	0.126(2)	0.429(1)
N2	-0.4380(7)	0.192(2)	0.428(1)
N3	-0.5679(8)	0.320(2)	0.441(1)
O1	-0.6220(6)	0.379(2)	0.449(1)
O2	-0.5454(6)	0.287(2)	0.3647(9)
C21	-0.5268(9)	0.266(2)	0.680(2)
C22	-0.5608(9)	0.302(3)	0.602(1)
C23	-0.5311(8)	0.272(3)	0.520(1)
C24	-0.4662(8)	0.219(2)	0.514(1)
C25	-0.4290(9)	0.184(2)	0.596(1)
C26	-0.4622(8)	0.208(3)	0.6731(1)
IODINE	-0.57073(7)	0.2940(3)	0.8049(1)

Table 7. Anisotropic Temperature Factors Obtained from the Diffractometer Data.

Atom	$B_{1,1}$	$B_{2,2}$	$B_{3,3}$	$B_{1,2}$	$B_{1,3}$	$B_{2,3}$
C1	0.0016(6)	0.052(7)	0.004(2)	0.002(2)	0.0004(7)	0.011(3)
C2	0.0005(7)	0.023(8)	0.008(2)	-0.001(2)	0.0006(9)	-0.002(3)
C3	0.0021(8)	0.017(7)	0.007(2)	0.001(2)	0.0010(9)	-0.000(3)
C4	0.004(1)	0.009(8)	0.014(3)	-0.003(2)	0.001(1)	0.001(4)
C5	0.0051(9)	0.018(7)	0.007(2)	0.003(2)	-0.003(1)	0.005(3)
C6	0.0052(8)	0.018(8)	0.004(2)	0.002(2)	-0.001(1)	0.004(4)
C7	0.008(1)	0.05(1)	0.004(2)	0.002(3)	0.001(1)	-0.001(4)
C8	0.006(2)	0.08(1)	0.016(3)	-0.007(4)	-0.001(2)	0.010(6)
C9	0.010(2)	0.05(1)	0.013(4)	-0.004(4)	-0.001(2)	0.009(5)
C10	0.010(1)	0.031(9)	0.003(2)	-0.006(3)	0.001(1)	-0.001(3)
C11	0.0029(8)	0.021(7)	0.006(2)	0.001(2)	0.0005(9)	0.004(3)
C12	0.007(1)	0.034(9)	0.010(2)	-0.003(2)	-0.004(2)	-0.000(5)
C13	0.007(1)	0.07(1)	0.007(3)	0.004(4)	-0.001(2)	-0.003(5)
C14	0.012(3)	0.12(2)	0.020(5)	-0.008(6)	-0.006(3)	-0.010(8)
C15	0.016(2)	0.14(2)	0.010(4)	0.020(7)	-0.004(2)	0.005(9)
N1	0.0022(6)	0.036(7)	0.006(2)	-0.000(2)	0.0015(7)	0.003(2)
N2	0.0020(5)	0.024(4)	0.006(1)	-0.001(2)	0.0019(6)	0.001(2)
N3	0.0018(6)	0.030(6)	0.008(2)	0.003(2)	0.0004(9)	0.000(3)
O1	0.0016(6)	0.053(6)	0.011(1)	0.003(1)	0.0000(7)	0.006(2)
O2	0.003(1)	0.061(6)	0.006(1)	0.002(2)	0.0000(6)	0.002(3)
C21	0.0034(6)	0.015(7)	0.010(2)	-0.003(2)	0.0027(9)	-0.004(3)
C22	0.0037(8)	0.031(7)	0.006(2)	-0.004(3)	0.0010(9)	-0.004(3)
C23	0.0014(5)	0.012(6)	0.005(1)	0.000(2)	0.0006(7)	0.001(3)
C24	0.0022(6)	0.008(6)	0.005(2)	0.000(2)	0.0013(7)	0.003(3)
C25	0.0026(5)	0.018(5)	0.005(1)	-0.005(2)	0.0003(8)	0.003(2)
C26	0.0019(5)	0.025(6)	0.006(2)	-0.000(2)	0.0008(7)	0.004(3)
I	0.00327(5)	0.0588(7)	0.0073(1)	-0.005(2)	0.0014(8)	-0.0015(3)

deviation in parenthesis.

Studies Directed Toward the Synthesis of Acorenone-B (10)

Synthesis of Methyl Pulegeneate (39) from Pulegone (38)

Pulegone[65] (38) was obtained from the spinning band distillation of pennyroyal oil.* GLC (flame) analysis of pennyroyal oil (3% Ucon LB-550X on 100/120 mesh Gas Chrom Q column, C.T. 130°, H.F.R. 85 ml/min) showed one major component (pulegone) with R_t 3.3 min (80%) and three other minor components with R_t 2.1 (1.5%), R_t 2.3 (1.5%), and R_t 9 min. (17%). GLC analysis of the spinning band fraction with b.p. 45°/0.4 mm, under the same conditions, showed one component with R_t 3.3 min (38, 99%).

Methyl pulegenate (39) was prepared** as described by Wolinsky and Chan.[66] Bromine (100 g) was added dropwise to a solution of pulegone (38, 108.3 g) in glacial acetic acid (150 ml) at 20°. After complete addition, the solution was stirred another thirty minutes at room temperature. The reaction mixture was poured on crushed ice and extracted with four 100-ml portions of petroleum ether (b.p. 35-40°, olefins were removed by concentrated sulfuric acid). The light-brown petroleum ether extract was washed with 5% sodium bicarbonate solution and water. The petroleum ether extract was dried over anhydrous $MgSO_4$ in the refrigerator. The dibromide of pulegone is unstable so that cold solutions and

*Pennyroyal oil (imported) was obtained from Fritzsche Brothers, Inc., New York.

**The preparation of methyl pulegenate by the method described by Achmad and G. W. K. Cavill[67] was also tried, but the procedure described here was found to be better.

the use of freshly prepared pulegone dibromide was essential to obtain high yields of methyl pulgenate (39).

Sodium (23 g) was added cautiously to anhydrous methanol (500 ml), which was obtained by distillation over magnesium methoxide. The freshly prepared petroleum ether extract was added dropwise to the sodium methoxide solution at 40°. The petroleum ether was distilled from the reaction mixture as the petroleum ether extract was added. After the addition was complete and the petroleum ether had distilled from the reaction mixture, the reaction mixture was heated at reflux for three hours. Then the reaction mixture was concentrated to one-half its original volume, cooled, and poured rapidly into 1 N hydrochloric acid (500 ml). The mixture was extracted with ether and the ether extract was washed with a 5% sodium bicarbonate solution and water. The ether extract was dried over anhydrous $MgSO_4$ and evaporated to give 87 g of a light yellow oil. The pulegone was removed from the oil by the Girard's "T" Reagent.* The oil (87 g) was added to a solution of Girard's "T" Reagent (60 g) in methanol (200 ml) and glacial acetic acid (30 ml) and refluxed for three hours. Then, the reaction mixture was concentrated, allowed to cool, and poured into a solution of sodium bicarbonate (25 g) in water (500 ml) and extracted with ether. The ethereal extract was washed with water, dried over anhydrous $MgSO_4$, and evaporated to give 35 g of methyl pulegenate (39).

The characterization and reactions of methylpulegenate was carried out on material prepared by K. Schorno[6] in a manner similar to that de-

*The Girard's "T" Reagent was obtained from Arapahoe Chemicals, Boulder, Colorado.

cribed in the preceeding section. GLC (flame) analysis of K. Schorno's methyl pulegenate (10% SE-30 on 80/100 mesh CW column, C.T. 160°, H.F.R. 85 ml/min) showed two major components with R_t 2.6 min (47%)* and with R_t 2.75 min (45%)* , and two minor components with R_t 2.3 min (2%)** and R_t 4.2 min (6%)* . The infrared spectrum of this material showed ν_{max}^{film} 1725 cm^{-1} (C=O). Schorno's[6] methyl pulegenate was vacuum distilled with a spinning band column at 35°/0.01 mm. GLC analysis of the distillate under the conditions described above showed only two peaks with R_t 2.6 min and R_t 2.75 min in a 1:1 ratio. The n.m.r. (CCl_4) spectrum of the (1:1) mixture showed signals at 58 (d, CH-$\underline{CH_3}$, J=6 cps), 60 (d, CH-$\underline{CH_3}$, J=6 cps), 98 (broad singlet, C=C-$\underline{CH_3}$, $W_{1/2}$ = 5 cps), and 216 cps (s, O-$\underline{CH_3}$, $W_{1/2}$ = 2 cps). The n.m.r. spectrum also contained unassigned multiplets at 112, 133, 172, 198, and 204 cps. The reported[66] n.m.r. spectrum for methyl cis-pulegenate showed signals at 60 (d, $\underline{CH_3}$CH, J=6 cps), 97 [$(\underline{CH_3})_2$C=C], 108 (m, $\underline{CH}$), 136 (m, $\underline{CH_2}$ and $\underline{CH_2}$-C=C), 198, 202 (C=C-CH-CO), and 216 (OCH_3). The reported n.m.r. spectrum for methyl trans pulegenate showed signals at 62 (d, $\underline{CH_3}$-CH, J=6 cps), 95, 100 [$(CH_3)_2$C=C], 115 (CH), 138 (m, CH_2 and C=C-$\underline{CH_2}$), 174 (C=C-$\underline{CH}$-CO), and 216 cps (OCH_3). The reported[66] infrared spectra of cis and trans methyl pulegenate showed carbonyl absorptions at 1724 cm^{-1}. Comparison of the n.m.r. spectra reported for cis and trans methyl pulegenates with the n.m.r. spectrum of the 1:1 mixture shows that it is a mixture of cis and trans methyl pulegenates. The infrared spectrum of the mixture of cis and trans methyl pulegenates showed ν_{max}^{film} 1725 cm^{-1}.

*The percentage given was estimated by relative peak heights.

Base (Sodium Hydride) Condensation of Methyl Pulegenate (39) with Dimethyl Carbonate: Preparation of Dimethyl 2-Isopropylidene-5-methylcyclopentane-1,1-dicarboxylate (40) and Dimethyl 2-Isopropyl-5-methylcyclopent-2-enedicarboxylate (41)

The reaction conditions were similar to those described by Corey.[68] The reaction conditions described below produced the best yield of the desired products. A 55 percent sodium hydride suspension in mineral oil (200 g) was washed with dry p-dioxane (distilled from sodium aluminum hydride) and added to dry p-dioxane (300 ml). Dry dimethyl carbonate (480 g, distilled from sodium) was added to the sodium hydride mixture under a positive pressure of nitrogen. The mixture was heated to 75°. Methyl pulegenate (92% of a 1:1 cis, trans mixture), which had been previously dried over anhydrous $MgSO_4$ in an ether solution and concentrated under vacuum, was added dropwise under nitrogen to the reaction mixture (75°). No appreciable change in the appearance of the reaction mixture was noted, so three drops of methanol were added and the mixture was heated to a vigorous reflux. After one hour a red color change was noted in the reaction mixture. The reaction mixture was refluxed for an additional twenty-four hours, cooled to 0°, and the excess sodium hydride was destroyed slowly with a glacial acetic acid-water (44:1) solvent mixture. The acidic solution was diluted with one liter of water and extracted with ether. The ethereal solution was washed with 5% sodium carbonate solution and water, dried over anhydrous $MgSO_4$, and evaporated to give a dark yellow oil. The oil contained mineral oil which had not been completely removed by washing the sodium hydride with dioxane. GLC (flame) analysis of the oil (10% SE-30 on 80/100

mesh CW column, C.T. 130°, H.F.R. 70 ml/min) showed a complex mixture; approximately* 80 percent of the material corresponded to peaks with retention times in the range of the uncondensed starting material (R_t 2.6-5.6 min) and 20 percent* of the material was contained in four peaks with longer retention times corresponding to possible condensation products (R_t 7.6 min, 2%; R_t 9.1 min, 6%; R_t 11.6 min, 2%; and R_t 13 min, 9%). Fractional vacuum distillation yielded 43.8 g of oil with b.p. 76-120°/0.1 mm and 17.6 g of oil with b.p. 128°/0.1 mm. GLC (flame) analysis (10% SE-30 on 80/100 mesh CW column, C.T. 160°, H.F.R. 80 ml/min of the fractions collected at 76-120°/0.1 mm showed that they contained a negligible amount of condensation products. GLC analysis of the fraction collected at 128°/0.1 mm showed that it contained two major components with R_t 4.45 min (34%) and R_t 6.4 min (33%) which corresponded to the peaks at R_t 9.1 min and R_t 13 min in the previous GLC analysis of the reaction mixture. Six other peaks made up the other 33 percent of the fraction collected at 128°/0.1 mm. Column chromatography of the oil ((b.p. 128°/0.1 mm, 15 g) on alumina (750 g) provided a crude separation of the two major condensation products. The residue (4 g) obtained from the hexane-benzene (4:1) eluent contained 80 percent of the component with R_t 4.45 min by GLC analysis. The residue (5 g) obtained from the hexane-benzene (1:1) eluent contained 90 percent of the component with R_t 6.4 min by GLC analysis.

Column chromatography of the residue (5 g) containing the component with R_t 6.4 min on alumina (75 g) yielded 460 mg of an oil (40, b.p.

*The percentage was estimated by relative peak heights.

93°/0.05 mm). GLC analysis of 40 showed only one peak with R_t 6.4 min. A total of 2.2 g of 40 (98% pure) was obtained from the chromatography. The infrared spectrum of 40 showed ν_{max}^{film} 1725 cm^{-1}. The n.m.r. (CCl_4) spectrum of 40 showed signals at 60 (3H, d, CH_3CH, J=7 cps), 95 (3H, m, $C=C-CH_3$), 101 (3H, m, $C=C-CH_3$), 219 (3H, s, OCH_3), and 221 cps (3H, s, OCH_3). The multiplet at 95 cps had the appearance of a poorly resolved unsymmetrical triplet with J=1.5-2.0 cps, whereas the signal at 101 cps has the appearance of a poorly resolved unsymmetrical triplet with J= 0.5 cps.

Anal. Calcd. for $C_{13}H_{20}O_4$: C, 64.97; H, 8.39

Found: C, 64.86; H, 8.43

Column chromatography of the residue (4 g) which contained the component with R_t 4.45 min, on alumina (200 g) yielded 200 mg of an oil (41, b.p. 80°/0.2 mm). The infrared spectrum of 41 showed ν_{max}^{film} 1725 cm^{-1}. The n.m.r. spectrum of 41 showed signals at 56 (3H, d, CH_3-CH, J=7 cps), 58 (3H, d, CH_3-CH, J=7 cps), 64 (3H, d, CH_3-CH, J=7 cps), 216 (3H, s, OCH_3, $W_{1/2}$ = 1 cps), 218 (3H, s, OCH_3, $W_{1/2}$ = 1 cps), and 337 cps (1H, t, C=C-H, J=2 cps).

Anal. Calcd.[6] for $C_{13}H_{20}O_4$: C, 64.97; H, 8.39

Found: C, 65.00; H, 8.65

Hydrogenation of 40: Preparation of Dimethyl 2-Isopropyl-5-methylcyclopentane-1,1-dicarboxylate (42)

Condensation product 40 (120 mg) was hydrogenated for 16 hours in glacial acetic acid with 5% Pt/C as the catalyst and with hydrogen at atmospheric pressure. The catalyst was removed by filtration using Celite filter aid; the filtrate was diluted with water and extracted with

ether. The ethereal extract was washed with a 5% sodium bicarbonate solution and water, dried over anhydrous $MgSO_4$, and evaporated to yield 100 mg of an oil (42, b.p. 54°/0.04 mm). GLC (flame) analysis of the oil (10' x 3/8" 10% SE-30 on 80/100 mesh CW column, C.T. 160°, H.F.R. 85 ml/min) showed one component with R_t 10.3 min (42). GLC analysis of 40 under the same conditions as described above showed one peak with R_t 9.5 min. The infrared spectrum of 42 showed ν_{max}^{film} 1725 cm^{-1} (C=O). The n.m.r. spectrum of 42 showed signals at 51 (3H, d, CH_3-CH, J=6 cps), 53.5 (3H, d, CH_3-CH, J=7 cps), 64 cps (3H, d, CH_3, J=6 cps), 221 cps (6H, s, OCH_3, $W_{1/2}$ = 2 cps). The mass spectrum of 42 gave a weak parent peak at m/e 242 (1%, calculated mol. wt. 242), the base peak at m/e 127, and a peak at m/e 211 (27%) which arises by loss of an O-CH_3 fragment.

Hydrogenation of 41: Preparation of 42

Condensation product 41 (100 mg) was hydrogenated for 16 hours in glacial acetic acid with 5% Pt/C (20 mg) as the catalyst and with hydrogen at atmospheric pressure. The catalyst was removed by filtration using Celite filter aid; the filtrate was diluted with water and extracted with ether. The ethereal extract was washed with a 5% sodium bicarbonate solution and water, dried over anhydrous $MgSO_4$, and evaporated to yield 90 mg of oil (42). GLC (flame) analysis of 42 (10% SE-30 on 80/100 mesh CW column, C.T. 150°, H.F.R. 80 ml/min) showed a single peak with R_t 4.0 min. GLC analysis of 41 by the same conditions as described above showed a single peak with R_t 3.8 min. A mixed injection of 41 and 42 gave two peaks. The infrared spectra of 42 obtained from two different sources (41 and 40) were superimposable. The n.m.r. spectrum of 42 obtained from two different sources (41 and 40) were superim-

posable. GLC analysis by the conditions described above showed that a mixed injection of 42 obtained from two different sources (41 and 42) gave one symmetrical peak with R_t 4.0 min. GLC (flame) analysis by mixed injection (15% 1,2,3-triscyanoxypropane on 60/70 mesh Gas Chrom P column, C.T. 155°, H.F.R. 85 ml/min) of 42 obtained from two different sources (41 and 40) gave one symmetrical peak with R_t 3.7 min.

Reduction ($LiAlH_4$) of Diester 42: Preparation of 2-Isopropyl-5-methyl-1,1-cyclopentanedimethanol (43)

Lithium aluminum hydride (50 mg) was added to anhydrous ether (40 ml). An ethereal solution of 42 (100 mg) was added dropwise to the well-stirred lithium aluminum hydride mixture. After the addition was complete, the reaction mixture was refluxed for three hours, then allowed to cool. The excess lithium aluminum hydride was destroyed by wet ether. The ethereal solution was decanted away from the lithium salts, washed with water, dried over anhydrous $MgSO_4$, and evaporated to yield 80 mg of an oil. GLC (flame) analysis of the oil (4' x 1/4" 3% Ucon LB-550X on 100/120 mesh Gas Chrom Q column, C.T. 155°, H.F.R. 90 ml/min) showed one peak with R_t 11.6 min. Vacuum distillation of the oil (100 mg) at 75°/0.01 mm yielded only 50 mg of oil. TLC analysis of the distillation product showed one dark spot with R_f 0.1 [benzene-hexane (1:9)] and a light spot with R_f 0.94.

The infrared spectrum (film) of the distillation product showed no carbonyl absorption and a strong hydroxyl absorption at 3350 cm^{-1}. Column chromatography of the oil (50 mg) on neutral alumina (15 g) gave 20 mg of an oil (43) in the chloroform-methanol (1:1) eluent. TLC analysis of 43 showed only one spot with R_f 0.1 [benzene-hexane (1:9)]. The

n.m.r. (CCl_4) spectrum of 43 showed signals at 53 (3H*, d, $CHC\underline{H}_3$, J=6 cps), 59 (3H*, d, $CHC\underline{H}_3$, J=6 cps), 64 (3H*, d, $CH\text{-}C\underline{H}_3$, J=6 cps), 170 (2H*, broad singlet, OH, $W_{1/2}$ = 5 cps), 203, 214, 221, 232 (2H*, doublet of doublets, $C\text{-}C\underline{H}_2\text{-}O$, J=11 cps), and 224 cps (2H*, s, $C\text{-}CH_2\text{-}O$, $W_{1/2}$ = 1.5 cps). The signal at 170 cps disappeared when the sample was mixed with D_2O. The low yield of material from the vacuum distillation and column chromatography could mean that 43 is easily polymerized.

Hydrogenation of Methyl Pulegenate (39): Preparation of Methyl 1-Isopropyl-5-methyl-1-carboxylate (44)

Methyl pulegenate (39), 10 g of a 1:1 cis, trans mixture) was hydrogenated for six hours in glacial acetic acid with 5% Pt/C (1 g) as the catalyst and with hydrogen at atmospheric pressure. The catalyst was removed by filtration using Celite filter aid; the filtrate was diluted with water and extracted with ether. The ethereal extract was washed with a 5% sodium bicarbonate solution and water, dried over anhydrous $MgSO_4$, and evaporated to yield 9.8 g of an oil (44). GLC (flame) analysis of 44 (10% SE-30 on 80/100 mesh CW column, C.T. 120°, H.F.R. 80 ml/min) showed one major peak with R_t 3.70 and a small shoulder with R_t 4.2 min. Under the same GLC conditions, the cis, trans mixture of methyl pulegenate showed two peaks with R_t 4.7 min and R_t 5.0 min. The infrared spectrum of 44 showed ν_{max}^{film} 1725 cm^{-1}.

Reaction of 44 with Dimethyl Carbonate and Sodium Hydride

Sodium hydride (8 g of a 55% suspension in mineral oil) was added to dry dioxane (50 ml distilled over sodium aluminum hydride). Dry di-

*Estimated.

methyl carbonate (10 g distilled over sodium) was added to the sodium hydride mixture and the mixture was heated to 75°. To this mixture, 40 (9 g vacuum distilled at 60°/10 mm) was added dropwise under a positive pressure of nitrogen. The mixture was heated to reflux. An aliquot was taken from the reaction mixture after 24 hours of reflux and acidified with glacial acetic acid. GLC (flame) analysis of the aliquot (6% SE-30 on 80/100 mesh CW column, C.T. 160°, H.F.R. 85 ml/min) showed two peaks with R_t 0.7 min and R_t 0.8 min but no other peaks. GLC analysis of 44 at the conditions described above gave one peak with R_t 0.8 min. After three days of reflux another aliquot was taken and GLC analysis at the conditions described above showed two peaks (approximately 1%) with R_t 2.6 min and R_t 3.4 min in addition to those at R_t 0.8 min and R_t 0.7 min. The peaks with R_t 2.6 min and 3.4 min could be condensation products so the reaction was refluxed for an additional two weeks under a positive pressure of nitrogen. No color change was noted in the reaction. The excess sodium hydride was destroyed with a glacial acetic acid-water (49:1) mixture. The acidic mixture was diluted with water and extracted with ether. The ethereal extract was washed with a 5% sodium carbonate solution and water, dried over anhydrous $MgSO_4$, and evaporated to yield an oil which contained mineral oil. Vacuum distillation at 54°/0.03 mm yielded 3.8 gm of a colorless oil. The infrared spectrum (film) of the distillate showed a weak absorption at 1700 cm^{-1} and a broad hydroxyl absorption at 3350 cm^{-1}. GLC (flame) analysis of the oil (3% OV-3 on 100/120 mesh CW column, C.T. 105°, H.F.R. 85 ml/min showed three peaks with R_t 3.8 min (32%)*, R_t 4.2 min (26%)* and R_t 4.6 min

*The peaks are not well therefore peak heights were used to estimate the relative percentages.

(42%).* No peaks were observed at longer retention time where the condensation products might be expected to appear. The mixture was not separated.

Reaction of 39 with Trityl Lithium and Methyl Chloroformate

The procedure for the preparation of trityl lithium was similar to the procedure used by Huff.[69] In a flame-dried apparatus under positive nitrogen pressure triphenylmethane (2.7 g) was dissolved in anhydrous dimethoxyethane (50 ml, distilled over sodium) at room temperature. A phenyl lithium solution (6 ml, approximately 1.8 M in ether) was added to the solution of triphenylmethane dropwise with a syringe. The deep red solution was stirred for thirty minutes. After thirty minutes, methyl pulegenate (39, 2 g) was added slowly to the deep red solution with a syringe. After most of 39 had been added, the solution changed from a deep red color to a light brown color. The solution was stirred for thirty minutes, then an excess of methyl chloroformate (6 ml) was added rapidly to the solution and the reaction mixture was stirred for another thirty minutes. The mixture was diluted with water and extracted with ether. The ethereal extract was washed with 5% sodium bicarbonate solution and water. GLC (flame) analysis of the ethereal extract (4' x 1/4" SE-30 on 80/100 mesh CW column, C.T. 125°, H.F.R. 85 ml/min) showed that most of the product was starting material with R_t 1.5 min and R_t 1.65 min (75%)*, with six other peaks accounting for the other material with R_t 2.6 min (7.5%), R_t 4.0 min (7.5%), R_t 4.8 min (6%), R_t 6.6 min (1%), R_t 8.0 min (1%) and R_t 9.6 min (0.5%). The condensation product 40 under

*The peaks are not well resolved therefore peak heights were used to estimate the relative percentages.

the same GLC conditions showed one peak with R_t 7.6 min. Since the amount of products formed with retention times in the range expected of 40 was small, the reaction was not investigated further.

CHAPTER IV

DISCUSSION OF RESULTS

Chemical Characterization of Acorenone-B

A new sesquiterpene, acorenone-B (10), has been isolated from the steam volatile oil of a hybrid grass derived from two races of the grass Bothriochloa intermedia. Acorenone-B was isolated from the essential oil by column chromatography.

The molecular formula of acorenone-B (10) $C_{15}H_{24}O$, was established by an elemental analysis and a precise mass determination. This molecular formula requires a structure with four double bonds and/or rings. The infrared spectrum of 10 (Plate I) contained a carbonyl absorption which is characteristic of an α,β-unsaturated ketone in a six-membered ring. The formation of a red 2,4-dinitrophenylhydrazone derivative (m.p. 151-152°) of 10 and the ultraviolet spectrum of 10 [λ_{max}^{MeOH} 240 mμ (ε = 16,300) and λ_{max}^{MeOH} 310 mμ (ε = 16.5)] also indicate the presence of an α,β-unsaturated carbonyl function. A comparison of the infrared spectrum of 10 with the infrared spectra of known sesquiterpenes[70] showed that the infrared spectrum of 10 was very similar to that of acorenone. Table 8 lists the physical properties of acorenone[5] and acorenone-B. In contrast with acorenone-B, acorenone would not form a 2,4-dinitrophenylhydrazone derivative. An authentic sample of an n.m.r. spectrum of acorenone was not available for direct comparison.

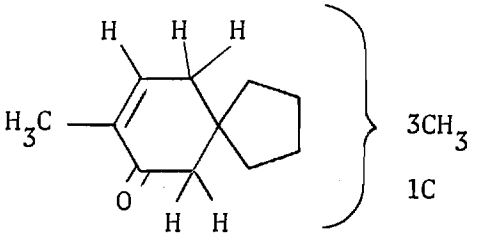
The n.m.r. spectrum of acorenone-B (10, Plate II) showed an ole-

Table 8. Comparison of Physical Properties of Acorenone[5] (3) and Acorenone-B (10).

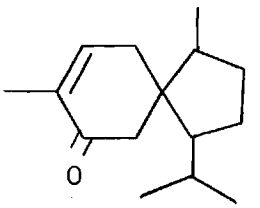
Compound	$[\alpha]_D^{20}$ (neat)	n_D	d
Acorenone	-22.3°	1.5039 (20°)	0.9599 (20°)
Acorenone-B (10)	-13.3°	1.4997 (30°)	0.9690 (30°)

finic proton (400 cps), an allylic methyl group (105 cps), and three secondary methyl groups (46, 52, 57 cps, J = 6 cps). The chemical shift of the vinylic proton is characteristic of a beta olefinic hydrogen.[71] The n.m.r. spectrum of 10 also showed a methylene group adjacent to the carbonyl group as a doublet of doublets (124, 141, 155, 172 cps, J = 17 cps). The relative intensities of signals one and two or signals three and four for this AB system can be readily calculated[72] from the J_{AB} and the absorption positions for the two A and B protons (see Appendix for the method of calculation). The calculated ratio of intensities for peaks one to two was 0.34; the observed (by peak height) ratio of intensities for signals one to two was 0.37. The appearance of the methylene protons as an AB doublet of doublets indicates that they are in different surroundings and are attached to a carbon adjacent to a quaternary carbon. The presence of an allylic methylene group is shown by a multiplet at 132 cps. Decoupling experiments indicated that the multiplet at 132 cps was coupled with the olefinic hydrogen at 400 cps. The n.m.r. evidence coupled with the infrared and ultraviolet spectra establishes the partial structure C. The partial structure C can be extended to 10 by ap-

plication of the Biogenetic Isoprene Rule.[9]



C



10

D. Arigoni[20] has isolated an alcohol from the mycelium of Fusidium coccineum, coccinol (11) by name. He has tentatively assigned the structure of a ketone derived from coccinol as that of acorenone-B[73] on the basis of a few chemical transformations, physiochemical investigations, and biogenetic reasoning.[20] D. Arigoni provided an n.m.r. spectrum of the coccinol ketone for comparison with the n.m.r. spectrum of 10 to help establish the structure of coccinol (11). A comparison of the two n.m.r. spectra is shown in Table 9. The two spectra are different, thus representing two different compounds. However, the comparison of the spectra does not rule out the possibility that 10 and the coccinol ketone are stereoisomers. The significant difference in the two spectra is in the multiplicity of the signals assigned to the CH_2-C=O and CH_2-C=C protons. In the acorenone-B case the CH_2-C=O protons are in widely different environments giving rise to a sharp quartet and the CH_2-C=C protons are a multiplet. The coccinol ketone case appears to be reverse of this, the CH_2-C=C protons are in widely different environments giving rise to a quartet of multiplets and the C-CH_2-C=O protons are a sharp singlet. The infrared spectrum of the coccinol ketone supplied by Arigoni was similar to the infrared spectrum of 10 with significant differences

Table 9. Comparison of the NMR Spectra of Acorenone-B and the Ketone Derived from Coccinol.[20]

Acorenone-B (10) cps	coupling	The Coccinol Ketone cps	coupling	Assignment
46	d, J=6 cps	43	d, J=6 cps	CH_3-CH
52	d, J=6 cps	53	d, J=6 cps	CH_3-CH
57	d, J=6 cps	59.5	d, J=6 cps	CH_3-CH
105	m	107	m	CH_3-C=C
147	q, J=16 cps	144	s	O=C-CH_2-C
132	m	140	q*, J=20 cps	C=CH-CH_2-C
400	m	400	m	C=CH

*This signal is a quartet of multiplets.

in the region of 8 to 10 μ. The ultraviolet spectrum [λ 242 mμ (ε = 6,000)] of the coccinol ketone has an anomalous low molar extinction coefficient. The ultraviolet spectrum [λ_{max}^{MeOH} 242 (ε = 16,300)] of acorenone-B (10) has a slightly high molar extinction as compared to 3,5,5-trimethyl-3-cyclohexen-1-one[74] [λ_{max}^{EtOH} 235 mμ (ε = 12,600)].

The principal degradation sequences of acorenone-B (10) are shown in Figure 8. The first sequence to be discussed is the hydrogenation of acorenone-B (10) to a dihydro product (25, $C_{15}H_{20}O$) using conditions (PtO_2/H_2, HOAc) described by Sorm[5] et al. for the hydrogenation of acorenone (3). The infrared spectrum of dihydroacorenone-B (25) contained a carbonyl absorption at 1710 cm^{-1} characteristic of a saturated ketone in a six-membered ring. The n.m.r. spectrum of 25 showed the absence

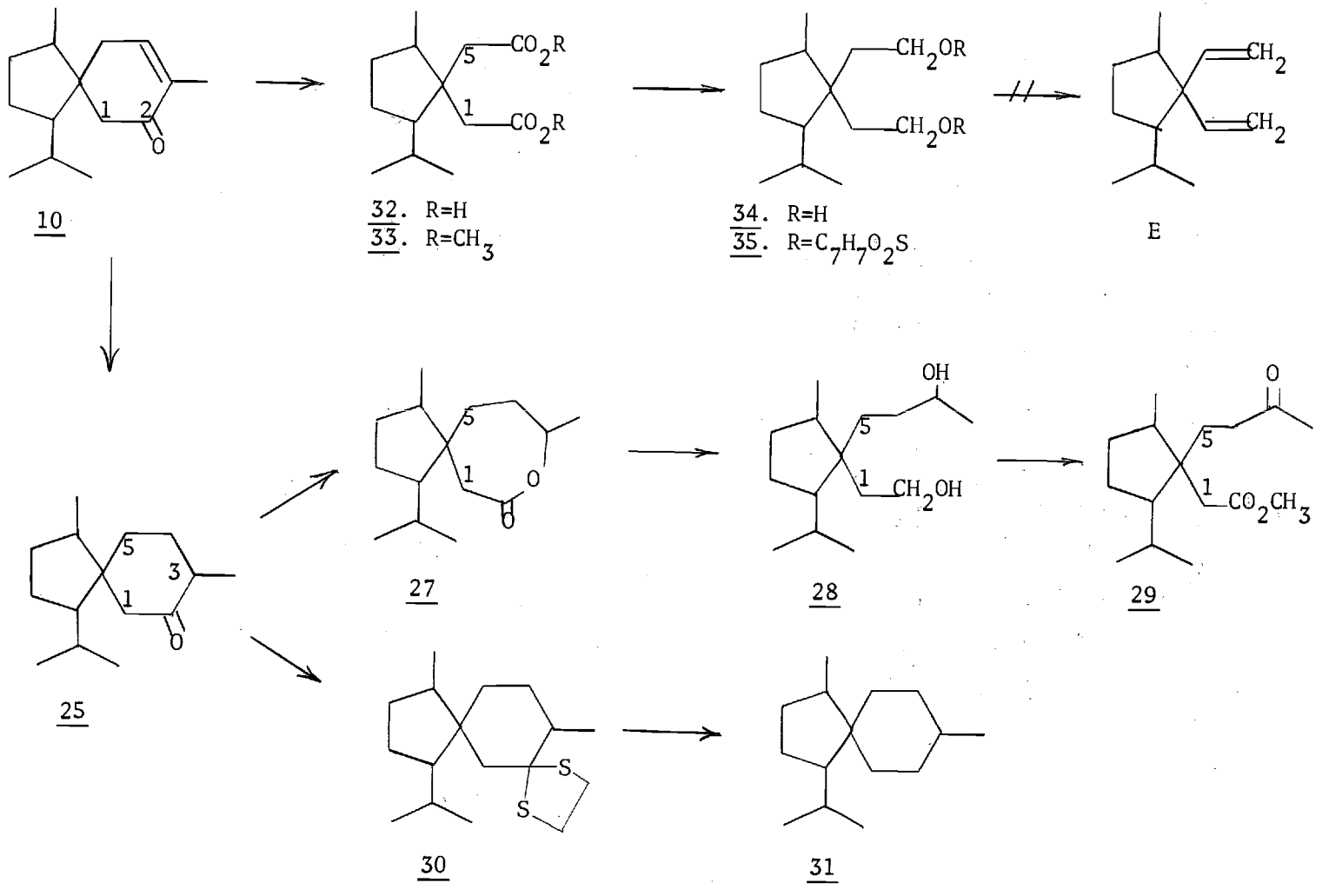


Figure 8. Degradation of Acorenone-B (10).

of olefinic protons, four secondary methyl groups, and an AB doublet of doublets (115, 129, 144, 158 cps, J = 14 cps) assigned to the methylene protons adjacent to the carbonyl. The observed (by peak height) ratio of intensities of peaks four to three was 0.40 in agreement with the calculated ratio of 0.35.

The infrared and n.m.r. spectra of 25 gave additional support to partial structure C. Dihydroacorenone-B (25) gave a yellow 2,4-dinitrophenylhydrazone derivative (m.p. 137-138°); but in contrast with dihydroacorenone (3), 25 would not yield a semicarbazone derivative.[5,6] GLC analysis showed that 25 was a mixture of two compounds (25a, 23% and 25b, 77%). The postulation that these two compounds are epimeric at C_3 is supported by equilibration studies and the difficulty encountered in the separation of the two compounds by chromatographic techniques. The sepataion of mixture 25 was achieved by preparative GLC using an analytical column. In this manner, a sufficient amount of material, enriched in 25a (1.5 mg, 85%) and 25b (4.65 mg, 97%), was obtained to run equilibration studies and ORD studies. The ORD and CD studies (described in another section) were run on the two enriched samples of 25a and 25b shortly after the samples were obtained; however, the equilibration of the samples was run a month later. The ease of equilibration of 25a and 25b is apparent as shown by their partial equilibration after standing one month at room temperature in methanol solution. Table 10 shows the results of the equilibration studies. The ratio of 25a to 25b after base equilibration ($NaOCH_3$) of fractions enriched in 25a and 25b was 32:68, which is similar to the mixture (23:77) obtained from the hydrogenation of acorenone-B.

Table 10. Equilibration of Dihydroacorenone-B (25).

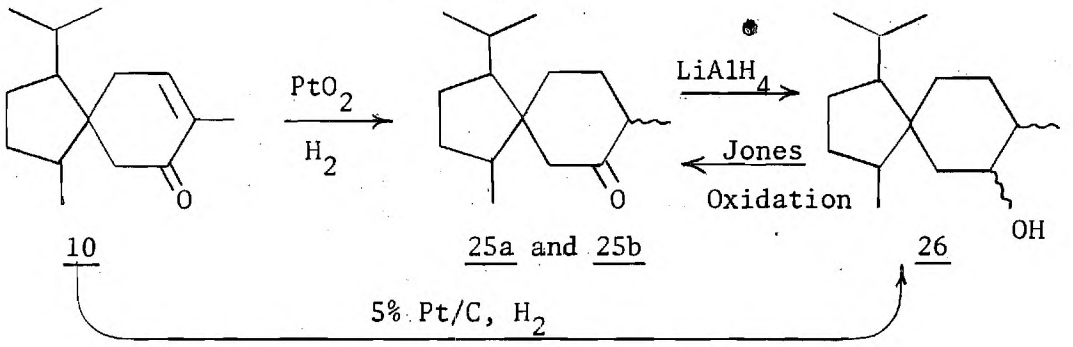
GLC Fraction	Initial Ratio (25a:25b)	Ratio after one month (25a:25b)	Ratio after Base Equiliartion (25a:25b)
1	85:15	70:30	32:68
3	3:97	11:89	32:68

An authentic sample of dihydroacorenone (12), supplied by V. Herout, was compared with dihydroacorenone-B (25) by GLC using the mixed injection technique. This comparison showed that dihydroacorenone (12) and dihydroacorenone-B (25) are different substances and that dihydroacorenone (12) is actually a mixture of two compounds (22.5% 12a and 77.5% 12b). Thus, acorenone (3) and acorenone-B (10) are two different compounds. The infrared spectrum of 12 was quite similar to 25 with differences in the region of 8-10 μ. The n.m.r. spectrum of 12 showed signals for the methyl protons which were nearly identical to those observed in the n.m.r. spectrum of 25, but in the region of 100-160 cps the two spectra were different. The mass spectra of 25 and 13 were similar, but gave different relative peak intensities.

If the hydrogenation (5%) Pt/C of acorenone-B (10) was carried out for an extended period of time, the reduction of the carbonyl group took place to yield a mixture of three alcohols. The major alcohol (26, 82.6%) was isolated by column chromatography. The infrared spectrum of 26 showed a strong hydroxyl absorption at 3300 cm^{-1}. The n.m.r. spectrum showed the presence of HCOH proton (226 cps) and a OH proton (184 cps) which was

reduced in intensity by the addition of D_2O. The parent peak (m/e 224) of the mass spectrum of 26 supported the molecular formula $C_{15}H_{28}O$. A peak at M^+-18 (m/e 206, 40%) was observed which corresponds to the loss of water from 26.

Jones[37] oxidation of alcohol 26 was carried out in an attempt to obtain one of the epimeric ketones (25a or 25b) in a pure form. However, the oxidation of 26 yielded the same mixture of saturated ketones (25) that had been previously obtained from the hydrogenation of acorenone-B (10).



Lithium aluminum hydride reduction of 25 yielded a mixture of three alcohols. GLC analysis showed that the major product (74%) of the reduction ($LiAlH_4$) corresponded to 26 which was isolated as the major product (84%) of the hydrogenation.

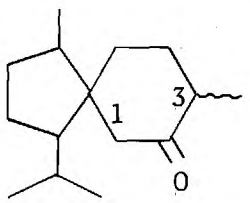
The complete reduction of acorenone-B (10) to the saturated hydrocarbon was accomplished via the thioketal derivative of 25. The reaction of 25 with 1,2-ethanedithiol in the presence of acid yielded the thioketal 30. The n.m.r. spectrum showed the thioketal ring protons (190 cps,

s), four secondary methyl groups (51, 52, 58, 67 cps, d, J = 6-7 cps), and the methylene protons adjacent to the thioketal function as a broad singlet (126 cps, $W_{1/2}$ = 4 cps). It is interesting to note that with the introduction of the thioketal function the methylene protons on the carbon adjacent to the thioketal function give rise to a singlet, whereas the corresponding methylene protons in 10 and 25 appeared as AB doublet of doublets. The introduction of the thioketal function apparently greatly reduces the nonequivalence of the surroundings of the methylene protons. A precise mass determination of 30 established its molecular formula as $C_{17}H_{28}S_2$.

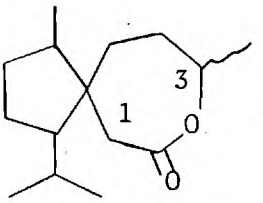
Thioketal 30 was reduced with lithium and ethylamine to yield hydrocarbon 31. The precise mass of 31 established the molecular formula of 31 as $C_{15}H_{28}$. The thick film infrared spectrum of the hydrocarbon 31 was very similar to the infrared spectrum of acorane[75] with slight differences in the region 8 to 9.8 μ. GLC analysis of 31 showed that the hydrocarbon was a mixture of two compounds, presumably epimeric at the C_3 carbon. Schorno[6] has reported that the same mixture of hydrocarbons was obtained from the hydrogenation of the olefins obtained from the dehydration of alcohol 26 with phosphorous oxychloride in pyridine.

The Baeyer-Villiger oxidation[38] of the saturated ketones (25) with trifluoroperacetic acid led to three products, one major product (73%) and two minor products (14% and 13%), by GLC analysis of the reaction mixture. The major product was obtained pure and was shown to be lactone 27 ($C_{15}H_{26}O_2$), since the two minor products were not obtained in pure form they were not characterized. However, one of the minor compounds is probably epimeric with 27 at the C_3 carbon since the Baeyer-Villiger re-

action is known[76] to involve migration with retention of configuration. The other minor product is probably lactone D, which could arise from the migration of the C_1 carbon instead of the C_3 carbon.

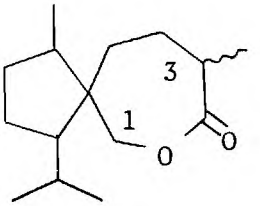


25



27

+



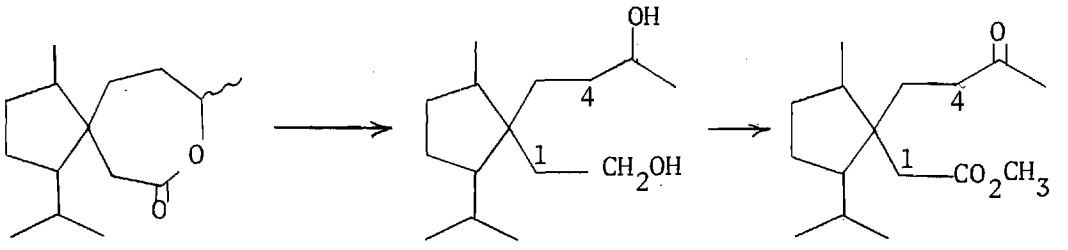
D

The infrared spectrum of the crystalline (m.p. 88.5-89°) lactone 27 shows a carbonyl absorption at 1700 cm^{-1} which is similar to the corresponding unsubstituted lactone (1704 cm^{-1}) derived from cyclohexanone.[77] The n.m.r. spectrum of 27 (Plate IV) showed four secondary methyl groups [52, 63*, 77 cps, J = 6-7 cps); the methyl group (77 cps) has been deshielded by the oxygen atom.] The proton attached to carbon C_3 appears as a multiplet centered at 264 cps. The methylene protons adjacent to the carbonyl group showed a doublet of doublets (113, 126, 183, 196 cps, J = 13 cps). The observed (by peak heights) ratio of intensities of peaks four to three was 0.68 in good agreement with the calculated ratio 0.70. It is interesting that there is a greater difference in chemical shifts of the two C_1 protons ($\Delta\nu_{AB}$ = 69 cps) than in the corresponding protons of acorenone-B ($\Delta\nu_{AB}$ = 26 cps) and dihydroacorenone-B ($\Delta\nu_{AB}$ = 27.6 cps). The n.m.r. spectrum of 27 supports the assigned structure.

*The signal at 63 cps contains two overlapping doublets.

Lithium aluminum hydride reduction of lactone 27 produced the diol 28 ($C_{15}H_{30}O_2$). Compound 28 was shown to be an alcohol by the strong hydroxyl absorption at 3350 cm^{-1} in its infrared spectrum and the broad two proton singlet (190 cps), which disappeared upon addition of D_2O, in the n.m.r. spectrum of 28.

The oxidation of 28 with chromium trioxide in glacial acetic acid followed by treatment with an ethereal solution of diazomethane produced ketoester 29 ($C_{16}H_{28}O_3$). The infrared spectrum of 29 showed the presence of two carbonyl absorptions; 1720 cm^{-1} for the methyl ketone functional group and 1730 cm^{-1} for the ester functional group. The n.m.r. spectrum of 29 showed a singlet (198 cps) for the methyl ester, a singlet (115 cps) for a methyl ketone, a broad singlet (132 cps) for the two C_1 protons, and a triplet (142 cps, J = 7 cps) for the two C_4 protons. The two most important features of this n.m.r. spectrum are the establishment of the presence of a methyl ketone function in 29 and the chemical shift of the C_1 protons which originated from the methylene group adjacent to the carbonyl group in acorenone-B (10). The presence of the methyl ketone function confirms the alpha position of the olefinic methyl group in acorenone-B (10). The importance of the chemical shift of the two C_1

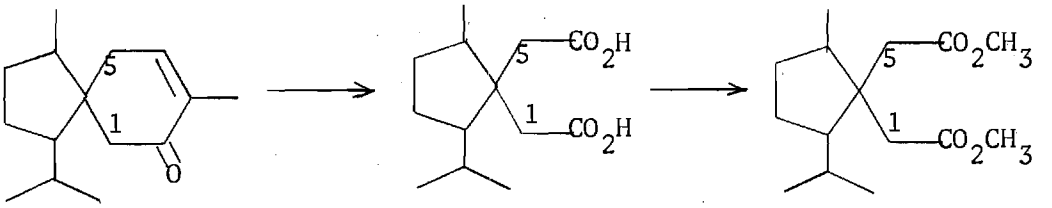


27 28 29

protons is discussed in connection with the ozonolysis of 10.

The ozonolysis of acorenone-B (10) by the procedure used by Sorm[5] et al. for the ozonolysis of acorenone (3) yielded crystalline diacid 32 ($C_{13}H_{22}O_4$) with m.p. 143-145°. Sorm[5] reported that the crystalline diacid obtained from the ozonolysis of acorenone had a melting point of 145-147°. The infrared spectrum of 32 showed broad absorption at 2500-2800 cm^{-1} characteristic of an acid, a carbonyl absorption at 1700 cm^{-1}, and the absence of absorption bands in the anhydride region (1750-1870 cm^{-1}). The n.m.r. spectrum of 32 showed a broad singlet (637 cps) for the acidic protons and two singlets (142 and 197 cps) for the two sets of protons on carbons C_1 and C_5. The mass spectrum of 32 did not give a parent peak (m/e 242) but gave a peak at m/e corresponding to the loss of one mole of water to form an anhydride. The conditions (analyzer 125°, 10^{-6}/mm) under which the analysis was made were conductive to anhydride formation.

Diacid 32 was esterified with an ethereal solution of diazomethane to yield diester 33 ($C_{15}H_{26}O_4$) with an optical rotation of $[\alpha]_D^{20}$ -7.9°. The infrared spectrum of 33 (Plate VI) showed a carbonyl absorption at 1730 cm^{-1}. The comparison of the infrared spectrum of 33 with



10 32 33

an infrared spectrum* of the dimethyl ester obtained from the degradation of acorenone showed that the two spectra were the same, within the limits imposed by comparing two spectra taken with different spectrophotometers. Thus, the metling point of the diacid 32 and the comparison of the infrared spectra of the diester degradation products indicate that the same compound was formed from the ozonolysis of acorenone-B (10) and acorenone (3). Since only the asymmetry of the spirane juncture is destroyed by ozonolysis, acorenone (3) and acorenone-B (10) would be epimeric about the spirane carbon juncture if their ozonolysis products are identical. Unfortunately a direct comparison of the ozonolysis products has not been possible; therefore, only a tentative assignment of the structure of acorenone (3) can be made from a complete knowledge of the structure of acorenone-B (10).

The n.m.r. spectrum of 33 (Plate VII) showed a broad singlet (199 cps, $W_{1/2}$ = 3 cps) for the methyl ester protons, a broad singlet (125 cps, $W_{1/2}$ = 3 cps) for the C_1 protons, and a broad singlet (158 cps, $W_{1/2}$ = 3 cps) for the C_5 protons. The assignment of the signal at 125 cps to the methylene protons originating from the C_1 protons of acorenone-B (10) was made on the basis of its similarity of chemical shift to the signal at 132 cps of ketoester 29. The origin of the methyl acetate residue in 29 is clearly the C_1, C_2 carbons of acorenone-B (10). Since the two methyl acetate residues of 33 are attached to the same carbon atom, the significant difference in chemical shift (33 cps) of the C_1 and the C_5 protons is probably due to the difference in steric environment. Bhacca and Williams[78] report that steric congestion can be respon-

*The infrared spectrum was kindly provided by Dr. V. Herout.

sible for deshielding effects of less than 60 cps. Since the C_5 protons are deshielded, these protons would be expected to be more sterically congested than the C_1 protons of 33. If the relative configuration of the isopropyl group and the methyl group of the cyclopentane ring was cis, the C_5 carbon would be expected to be cis to the methyl and isopropyl groups. If the methyl group and the isopropyl group were trans, then no clear conclusion about the relative stereochemistry of the C_1 or the C_5 carbons could be made.

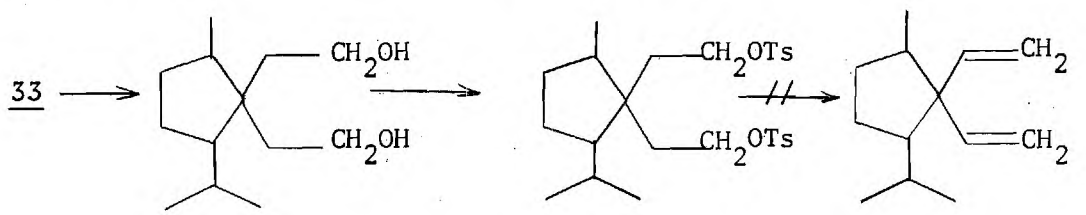
An attempt to degrade diester 33 to a cyclopentane derivative with known stereochemistry was made by the lithium aluminum hydride reduction of 33 to the crystalline diol 34. The infrared spectrum of 34 showed a strong hydroxyl absorption at 3350 cm^{-1} and the absence of carbonyl absorption. The n.m.r. spectrum of 34 showed the two hydroxyl protons as a broad singlet (160 cps) and a multiplet (205-240 cps) for the CH_2OH protons. The mass spectrum gave a parent peak at m/e 214 and also a peak due to the loss of two moles of water (m/e 178, 50%).

The crystalline tosylate (m.p. 78-79°) of 34 was prepared from p-toulenesulfonylchloride in pyridine. The infrared spectrum of 35 showed an absorption at 1605 cm^{-1} characteristic of a tosylate and the absence of hydroxyl absorption. The n.m.r. spectrum of ditosylate 35 showed a doublet of doublets (450, 458, 476, 473) for the aromatic protons, two triplets (243, 245 cps) for the C_5 and C_2 protons, and a triplet* (101 cps) for the C_1 and C_6 protons. Decoupling experiments indicated that the two triplets at 243 and 245 cps were coupled with the triplet at 101 cps.

*The triplet at 101 cps was partially obscured.

The elimination of a tosylate by elution through basic alumina was tried with a model compound, 1-decanol tosylate, and found to give a good yield of 1-decene.

However, ditosylate 35 did not readily suffer elimination under the same conditions. The desired product E was not obtained.



34 35 E

At this point in the degradative sequence a suitable derivative of acorenone-B for X-ray analysis was obtained, so that the final proof of the spirane structure and relative stereochemistry of acorenone-B was obtained from the X-ray structure determination.

Studies in the Preparation of a Crystalline Derivative for X-ray Analysis

The preparation of a crystal for single crystal X-ray analysis was approached so that the heavy atom method[53] could be used for the structure determination. Although the heavy atom method does not give quite as accurate atomic positions as the direct method, the heavy atom method requires less sophisticated computer techniques. The introduction of a heavy atom (an atom with several times the atomic number of carbon) also provides the possibility of determining the absolute configuration of the molecule. The halogens, bromine and iodine, are usually the most convenient source of heavy atoms for organic structures.

The preparation of the p-bromophenylsulfonylhydrazone derivative of acorenone-B (10) was not successful using several different reaction conditions. The failure of acorenone-B (10) to form a derivative of p-bromophenylsulfonylhydrazide is in contrast with the formation of acorone p-bromophenylsulfonylhydrazone which was used for the X-ray structure determination of acorone[18].

p-Iodobenzoylhydrazide has been described[42] as a good compound for the formation of α,β-unsaturated ketone derivatives. p-Iodobenzoylhydrazide was prepared from p-iodotoluene by a previously reported procedure[42]. The melting points of p-Iodobenzoylhydrazide and the intermediate compounds in the synthesis were the same as reported in the literature.[42] The n.m.r. spectrum of p-iodobenzoylhydrazide showed broad signals at 270 and 590 cps for the O=CNH-NH_2 and O=CNH-NH_2 protons, respectively, and a doublet of doublets for the four aromatic protons (454, 462, 468, 476 cps). Neither acorenone-B (10) nor dihydroacorenone-B (25) gave suitable p-iodobenzoylhydrazide derivatives for X-ray work. A precipitate formed during the reaction of both 10 and 25, but this precipitate decomposed at 320° and attempts to recrystallize it failed. This precipitate was not further characterized.

The reduction of acorenone-B (10) with sodium borohydride provided an alcohol degradation product with the introduction of only one new asymmetric center. The reduction of a small amount of 10 produced a mixture of two alcohols (37), presumably epimeric at the C_2 carbon. The two alcohols (37) were not separated or purified before further reaction, because hopefully the iodoacetate would be a solid derivative and easily purified. The infrared spectrum of 37 showed a strong

hydroxyl absorption and the absence of carbonyl absorption. The n.m.r. spectrum of 37 showed a multiplet of 325 cps for the olefinic proton and multiplets at 295 and 200-260 cps, which is in the region expected for the chemical shift of the hydroxyl and CH-OH protons.

The iodoacetate of 37 was prepared via the chloroacetate of 37. The chloroacetate of 37 was prepared from 37 and α-chloroacetylanhydride in dry pyridine. The infrared spectrum of the product showed an absence of hydroxyl absorption and the presence of a broad carbonyl absorption at 1725 cm^{-1}, which indicated that the chloroacetate of 37 had been formed. The chloroacetate of 37 was refluxed in dry acetone with sodium iodide to form the iodoacetate of 37. GLC analyses of the reaction product revealed two major components which comprised approximately 70 percent of the mixture. The n.m.r. spectrum of the crude mixture showed a broad signal at 220 cps which is in the region of chemical shift expected for the O=C-CH_2-I protons. However, a solid was not obtained and further purification of the mixture was not pursued.

Three disubstituted phenylhydrazines (4-iodo-2-nitrophenylhydrazine, 2-iodo-4-nitrophenylhydrazine, 2-iodo-4-nitrophenylhydrazine, and 5-iodo-2-nitrophenylhydrazine) were prepared and reacted with acorenone-B (10) to see which compound would form the best derivative for the X-ray structure determination. Of the three hydrazines, 4-iodo-2-nitrophenylhydrazine formed a derivative with the minimum number of side products; thus, this was the derivative used for the X-ray studies. The phenylhydrazines were obtained by following procedures described in the literature.[44-48] Acorenone-B (10) was treated with 4-iodo-2-nitrophenylhydrazine in 95 percent ethanol containing one drop of sulfuric acid to

form acorenone-B 4-iodo-2-nitrophenylhydrazone (36). TLC analysis of the reaction mixture showed three spots, which corresponded to 10, 4-iodo-2-nitrophenylhydrazine, and 36. The reaction mixture was chromatographed on an alumina column to obtain pure 36 which crystallized after considerable difficulty, m.p. 89-90°. The infrared spectrum of 36 (see Plate IX) showed N-H absorption at 3310 cm^{-1}. The ultraviolet spectrum of 36 showed: λ_{max}^{MeOH} 465 mμ (ε = 6,700), λ_{max}^{MeOH} 314 mμ (ε=21,000), and λ_{max}^{MeOH} 266 mμ (ε = 21,000). The n.m.r. spectrum 36 (Plate VIII) showed a multiplet at 348 cps for the olefinic hydrogen, two singlets for the aromatic protons (442 cps, 2H; 486 cps, 1H), and a singlet at 630 cps for the N-H proton. The n.m.r. spectrum in the region of the methyl protons was poorly resolved. Crystals of 36 suitable for X-ray single crystal analysis were obtained from a supersaturated benzene-95 percent ethanol (3:17) solution at 43°.

X-ray Crystal Structure of Acorenone-B 4-Iodo-2-nitrophenylhydrazone (36)

Two sets of data were collected and refined on the same crystal of acorenone-B 4-iodo-2-nitrophenylhydrazone (36). The film data was used to obtain the structure of 36 and the diffractometer data was used to obtain the additional accuracy needed for the determination of the absolute configuration of 36. Both sets of data yielded the same structure; as expected, the diffractometer data refined to a lower R value. Since the diffractometer data was more complete, the discussion of the details of the structure will be based on the final parameters obtained from the final refinement (R = 0.057) of the diffractometer data.

The view of 36 shown in Figure 9 gives the general features of the structure of acorenone-B 4-iodo-2-nitrophenylhydrazone (36). The chemically postulated ortho position of the nitro group (N_3, O_1, O_2) and the para position of the iodine atom on the benzene ring (C_{21}-C_{26}) have been confirmed. Figure 9 also shows that the acorenone-B portion of the molecule (36) has the spiro[4.5]decane structure (C_1-C_{10}). The positions of the methyl group (C_{11}) on the cyclohexane ring and the methyl group (C_{12}) and the isopropyl group (C_{13}-C_{15}) on the cyclopentane ring are consistent with the acorane type of hydrocarbon skeleton.

Tables 11 and 12 list the bond distances and angles of the structure, respectively, with the estimated standard deviation[79] in parenthesis. All of the bond distances are within three estimated standard deviations of generally accepted values except for C_9-C_{10} (1.75 Å) of the cyclopentane ring and C_{24}-C_{25} (1.47 Å) of the benzene ring. These bond lengths are probably somewhat longer than their true values. Random errors, an incomplete set of data, and the presence of some systematic errors due to absorption and detector counting losses will tend to accentuate variations in bond length. However, the consistently long bond lengths associated with the cyclopentane ring and its substituents may represent a true bond extension of the 1.536 Å value for ethane. Oh and Malsen[80] report a bond extension of 0.02 Å for highly substituted sp^3 carbon-carbon bonds. The mechanism for the bond extension is not known with certainty, but non-bonded steric repulsion may be the principal factor.[80] The bond angles which deviate from the generally accepted value probably do not represent their true values. The variations in the bond angles are probably accentuated

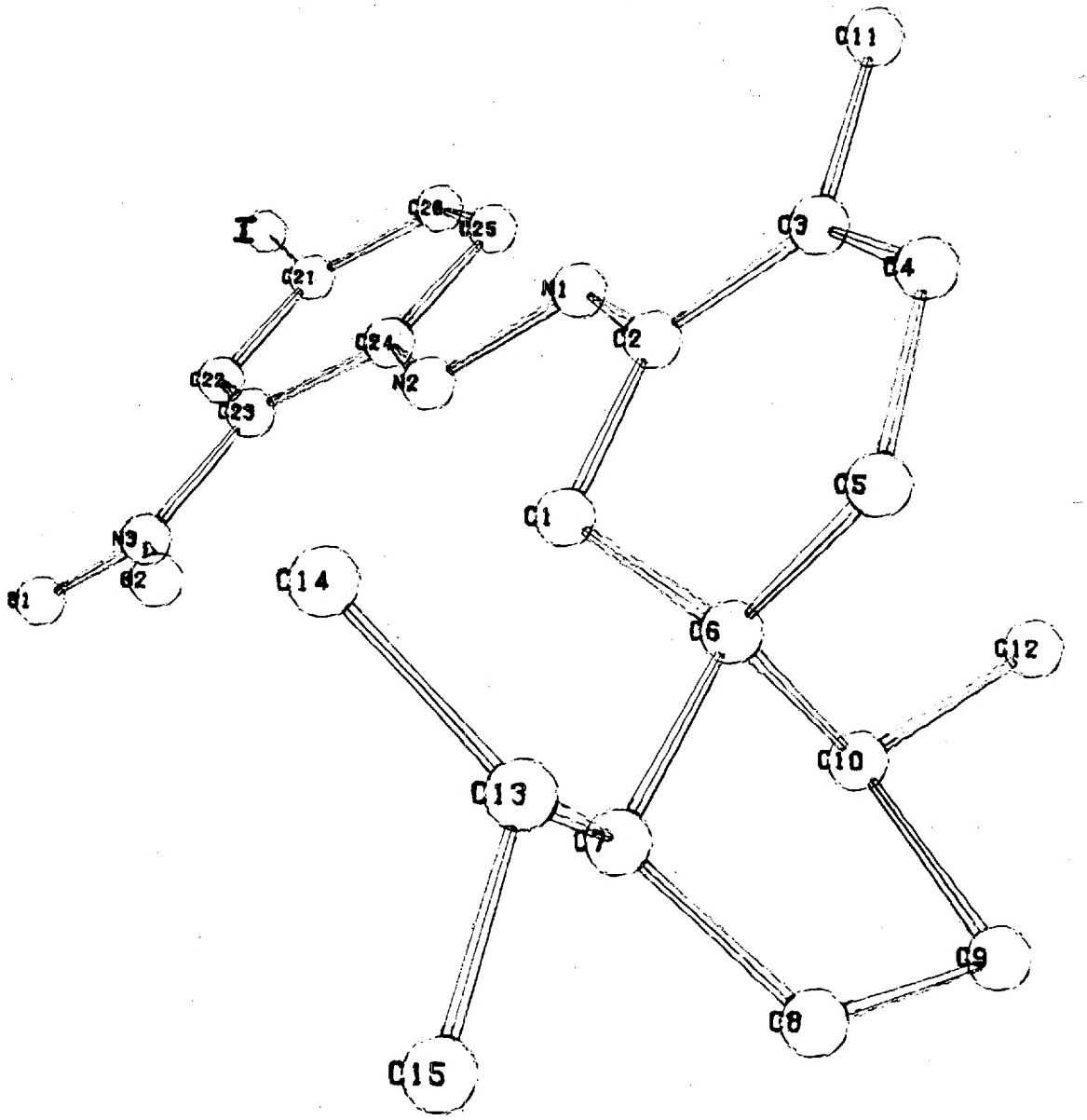


Figure 9. Perspective Drawing of 4-Iodo-2-nitrophenylhydrazone (36).

Table 11. Bond Distances from the Final Refinement

Bonds	Distance, Å	Bonds	Distance, Å
C1-C2	1.53(2)	C13-C14	1.61(5)
C2-C3	1.43(2)	C13-C15	1.58(4)
C3-C4	1.42(3)	C2-N1	1.27(2)
C4-C5	1.60(3)	N1-N2	1.40(2)
C5-C6	1.59(2)	N2-C24	1.41(2)
C1-C6	1.54(2)	N3-C23	1.44(2)
C6-C7	1.64(3)	N3-O1	1.21(2)
C6-C10	1.56(3)	N3-O2	1.24(1)
C7-C8	1.57(3)	C21-C22	1.38(2)
C8-C9	1.61(4)	C22-C23	1.37(2)
C9-C10	1.75(4)	C23-C24	1.41(2)
C10-C12	1.61(3)	C24-C25	1.47(2)
C3-C11	1.55(3)	C25-C26	1.33(2)
C7-C13	1.60(3)	C26-C21	1.41(2)
		C21-Iodine	2.07(2)

Table 12. Selected Angles from the Final Refinement

Bonds	Angle, in degrees	Bonds	Angle, in degrees
C3-C2-C1	122(2)	C11-C3-C4	119(2)
C2-C3-C4	120(2)	C11-C3-C2	120(2)
C3-C4-C5	124(2)	N1-C2-C1	120(2)
C4-C5-C6	109(2)	N1-C2-C3	118(2)
C5-C6-C1	116(2)	N2-C16-C2	118(2)
C6-C1-C2	111(2)	C24-N2-N1	115(2)
C1-C6-C7	109(2)	C21-C22-C23	119(2)
C1-C6-C10	109(2)	C22-C23-C24	122(2)
C5-C6-C7	110(2)	C23-C24-C25	120(2)
C5-C6-C10	114(2)	C24-C25-C26	114(2)
C7-C6-C10	97(2)	C24-C25-C26	114(2)
C6-C7-C8	106(2)	C26-C21-C22	119(2)
C7-C8-C9	109(3)	N2-C24-C25	121(2)
C8-C9-C10	98(2)	N2-C24-C23	120(2)
C9-C10-C6	104(2)	N3-C23-C22	116(2)
C6-C10-C12	117(2)	N3-C23-C24	122(2)
C6-C7-C13	114(2)	O2-N3-C23	119(2)
C7-C13-C15	102(3)	O1-N3-C23	120(2)
C7-C13-C14	108(2)	O1-N3-O2	121(2)
C14-C13-C15	121(3)	I-C21-C26	121(2)
		I-C21-C22	120(1)

by the errors mentioned above.

Figure 10 gives a closer view of the acorenone-B portion of 36. The atoms are represented by thermal ellipsoids which are calculated[81] from the anisotropic temperature factors and plotted with an off-line Calcomp Plotter. In this view the methyl group (C_{12}) and the isopropyl (C_{13}-C_{15}) group attached to the cyclopentane ring are clearly cis. The methylene group (C_5) adjacent to the double bond has a cis relationship to the methyl and isopropyl group. This is consistent with the assignment of the low field methyl acetate residue of 33 to the sterically congested cis relationship to the methyl and isopropyl groups. Since acorenone (3) has been tentatively assigned the same sterochemistry as acorenone-B (10), except for the spirane juncture, on the basis of the comparison of ozonolysis products, the carbonyl group of acorenone (3) would have a cis relationship to the methyl and isopropyl groups of the cyclopentane ring. The sterically congested cis relationship of the carbonyl function in acorenone (3) might explain the failure of acorenone (3) to form a 2,4-dinitrophenylhydrazone derivative[5], whereas acorenone-B (10) readily forms a 2,4-dinitrophenylhydrazone derivative.

The conformation of the cyclopentane ring and the relative configuration of the methyl and isopropyl groups were also analyzed by calculating the least squares plane of atoms C_7-C_{10} of the cyclopentane ring and the distance of atoms C_{12}, C_{13} and C_6 from this plane. Table 13 lists the values obtained from the least squares calculation[82] of the cyclopentane ring. The cyclopentane ring is in the envelope conformation where atoms C_7-C_{10} are in essentially one plane ($\pm$ 0.05 Å) and the C_6 atom is displaced from the plane by -0.77 Å. The methyl group (C_{12})

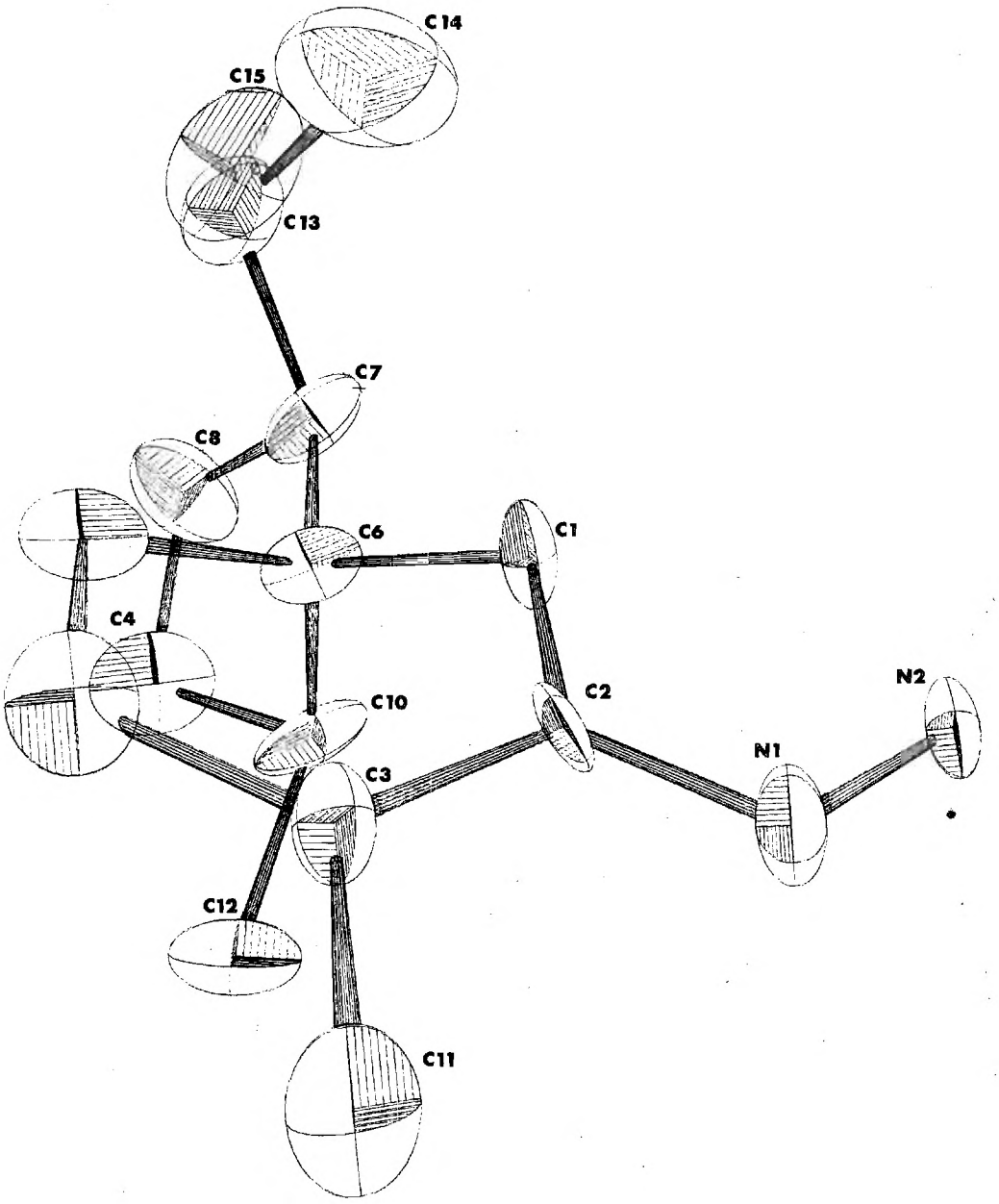


Figure 10. Acorenone-B Portion* of 36 with the Thermal Ellipsoids Represented.

*In this view C_{15} of the isopropyl group is partially hidden by C_{13} of the isopropyl group and the cyclohexane ring C_1-C_6 is projecting out of the plane of the paper and the cyclopentane ring C_6-C_{10} is projected into the plane of the paper.

and the central isopropyl carbon (C_{13}) are displaced from the plane by -0.63 Å and -0.91 Å, respectively. The same sign indicates that the atoms are all displaced from the plane in the same direction, thus confirming the cis relationship of C_{12} and C_{13}. The envelope conformation is the usual conformation encountered in crystal-structure studies of five-membered rings;[18] however, it is in contrast with the half-chair conformation of the cyclopentanone ring system in acorone.[18] The isopropyl and methyl groups of the cyclopentanone ring are in a trans relationship in acorone.[18] The methylene group adjacent to the carbonyl group of acorone has a cis relationship to the methyl group attached to the cyclopentanone group; whereas in 36 the corresponding methylene group has a trans relationship to the methyl group attached to the cyclopentane ring.

Table 14 gives the least squares plane formed by atoms C_1-C_5 of the cyclohexane ring. These atoms would be expected to be planar for good π overlap of the conjugated system. Atoms C_1-C_5 deviate by $\pm$ 0.05 Å from the least squares plane. Atom C_6 of the cyclohexane ring is puckered and is displaced by -0.57 Å from the least squares plane.

Table 15 gives the least squares plane formed by the atom of the benzene ring (C_{21}-C_{26}). The deviation of atoms (C_{21}-C_{26}) from the least squares plane is only $\pm$ 0.02 Å. The deviations of the atoms substituted on the benzene ring are consistent with a planar model.

The relatively large size of the thermal ellipsoids (Figure 10) representing the atoms of the cyclopentane ring and its substituents indicate the high thermal motion of these atoms within the crystal.

Table 13. Least Squares Plane* of the Cyclopentane Ring: -0.649X + 0.760Y + 0.443Z -6.72 = 0.

Atom	Distance, A	Atom	Distance, A
C_7^{**}	-0.033	C_{12}	-0.633
C_8^{**}	+0.053	C_{13}	-0.911
C_9^{**}	-0.051	C_6	-0.773
C_{10}^{**}	+0.031		

Table 14. Least Squares Plane* of the Cyclohexane Ring: -0.386X -0.893Y -0.232Z -0.768 = 0.

Atom	Distance, A	Atom	Distance, A
C1**	+0.042	C5**	-0.046
C2**	-0.026	C6	-0.567
C3**	-0.024	C11	-0.044
C4**	+0.055	N1	+0.111

*All planes are expressed in Cartesian coordinates. The transformations are: X = xa, Y = ya, Z = za.

**A plane is derived using unit weights for atoms with double astericks.

Table 15. Least Squares Plane* of the Benzene Ring: -0.292X -0.956Y -0.0138Z -1.23 = 0.

Atom	Distance, A	Atom	Distance, A
C_{21}^{**}	+0.005	Iodine	+0.053
C_{22}^{**}	-0.020	N_2	+0.022
C_{23}^{**}	+0.021	N_3	-0.070
C_{24}^{**}	-0.005	O_1	-0.145
C_{25}^{**}	-0.012	O_2	+0.035
C_{26}^{**}	+0.011		

*All planes are expressed in Cartesian coordinates. The transformations are: X = xa, Y = ya, Z = za.

**A plane is derived using unit weights for atoms with astericks.

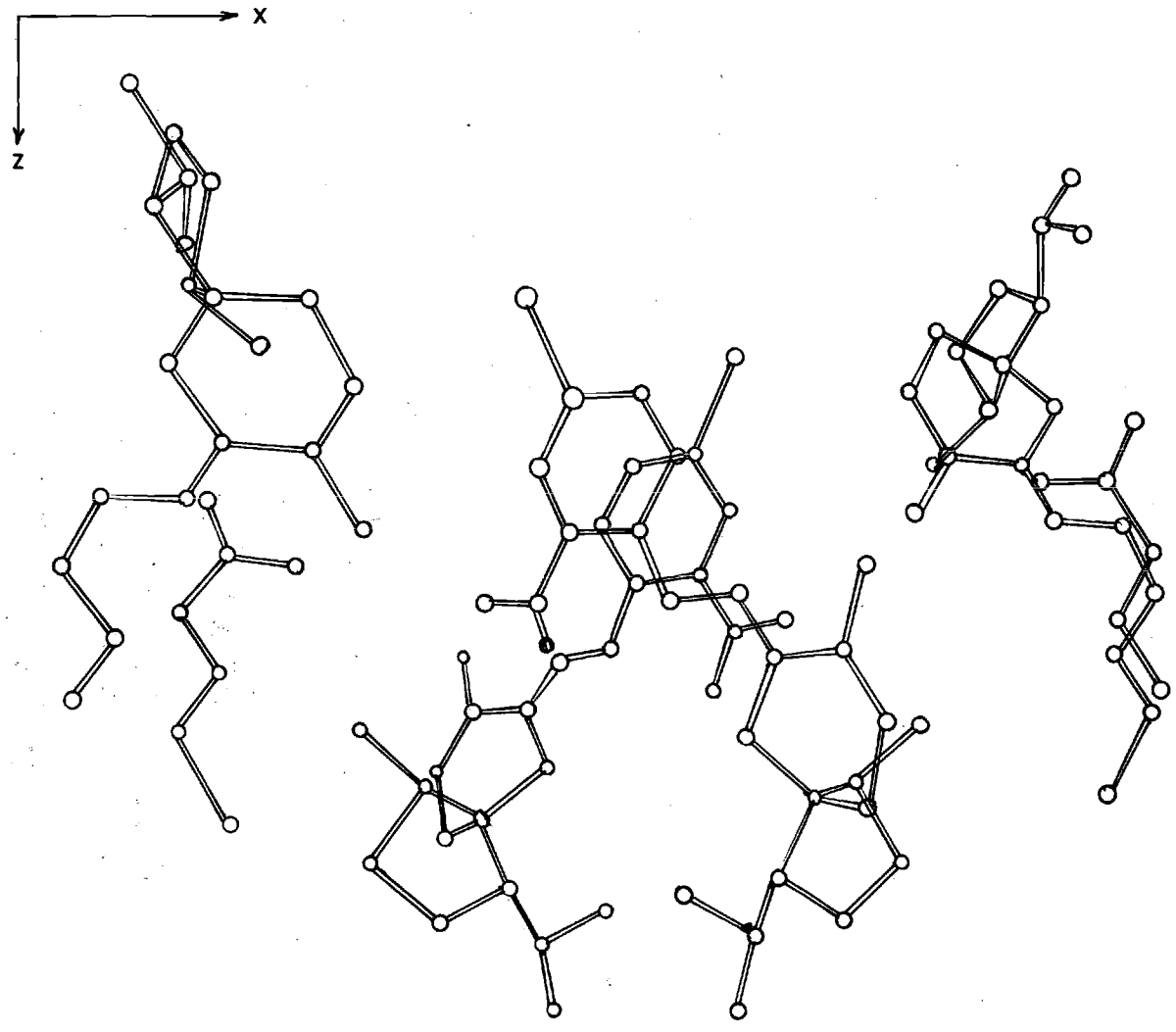


Figure 11. Packing Diagram of Two Molecules of 36 and Portions of the Neighboring Molecules in the Unit Cell.

These high thermal parameters may be partly responsible for the somewhat rapid fall-off of intensities with increasing angles of scattering.[83] Only reflections with Miller indices up to h = 22, k - 6, and $\underline{1}$ = 14 were observed; whereas, indices up to h = 58, k = 20, $\underline{1}$ = 41 are within the Mo K_α sphere of the reflection. Figure 11 shows a packing diagram of the unit cell of 36. This shows that the acorenone-B portion of the molecule is rather loosely packed. Also, Drieding models of acorenone-B indicate that the cyclopentane ring and its substituents are quite flexible compared to the cyclohexane portion of the molecule.

The absolute configuration of 36 and therefore acorenone-B has been determined by two methods, Hamilton's[61] R factor significance test and the comparison of Bijvoet[64] pairs. Figures 9-11 represent the correct absolute configuration of acorenone-B.

ORD and CD Studies of Acorenone-B (10) and its Degradation Products.

The results of the ORD and CD studies are given in Table 16. The purpose of the ORD and CD studies was to lend support to the absolute configuration of acorenone-B (10), which was determined by X-ray analysis. Table 16 shows that there were two Cotton effects associated with 10, a + 18.7 for the $n \rightarrow \pi^*$ transition and a -115 for the $\pi \rightarrow \pi^*$ transition. Both the $n \rightarrow \pi^*$ and the $\pi \rightarrow \pi^*$ transitions are known to reflect the chirality of the C=C–C=O chromophore[84,34]. However, Kuriyama[86] suggests that the sensitivity of the Cotton effects of α,β-unsaturated ketones to very subtle interactions strongly suggests that much caution should be exercised when correlating the Cotton effects of such substances with their structures. An examination of

Table 16. ORD, CD and Ultraviolet Spectra of Degradation Products of Acorenone-B (10).

Compound	CD		ORD		a	UV
	wave length (mμ) of maxima	[Θ]	wave length (mμ) at [Φ] ±0°	a	calculated from CD*	wavelength (mμ), ε in parenthesis
10 ($n\rightarrow\pi^*$)	322	+1,530			+18.7	310 (16)
10 ($\pi\rightarrow\pi^*$)	237	-7,400	240	-115	-90.5	242 (16,300)
25a (85%)	295	+580	287	+9.9	+7.1	278 (22)
25b (97%)	292	+1,510	294	+22	+18.5	283 (26)
27	225	+3030	232	+53	+36	218 (98)
29	285	-276	294	-2.9	-3.3	279 (53.5) 273 (156)
Dihydro-acorenone	296	-670	298	-8.85		

*See appendix for method of calculation.

the Dreiding models of the two possible enantiomers (A and B) of acorenone-B does not reveal any preference of one chirality over the other for the two possible enantioners (A and B).

The two epimeric saturated ketone derivatives (25a and 25b) were separated into two fractions containing 85 percent 25a and 97 percent 25b, respectively. Since the octant rule is well established for the saturated carbonyl, it was hoped that the investigation of these two epimers would lead to some definitive results. Also, base equilibration studies established that epimer 25b was somewhat more stable than epimer 25a (the ratio of 25b/25a at the equilibrium was 68:22). The results of the ORD and CD measurements show that 25a and 25b both show rather weak Cotton effects, a + 22 and a + 9.9 respectively. The two possible epimers of 25 and the octant projections of the conformations which by inspection of Drieding models seem to be of lowest energy are shown in Figure 12. The anomalous feature of the ORD and CD curves of 25a and 25b is that both give weak positive Cotton effects. If the cyclohexane ring adopted the chair conformation with the methyl group in the equatorial position in both epimers, then in one case (V) a strong negative Cotton effect would be expected and in the other case (W) a strong positive Cotton effect would be expected (Figure 12). Since this was not observed, the ORD and CD of 25a and 25b represent a more complex situation. G. Snatzke[86] has observed that conformational flexibility may lower the amplitude of the Cotton effect. Conformational equilibrium is also known[87] to reduce the amplitude of the Cotton effect. The presence of fine structure in the ORD and CD spectra of 25a and 25b indicates that there may be an equilibrium

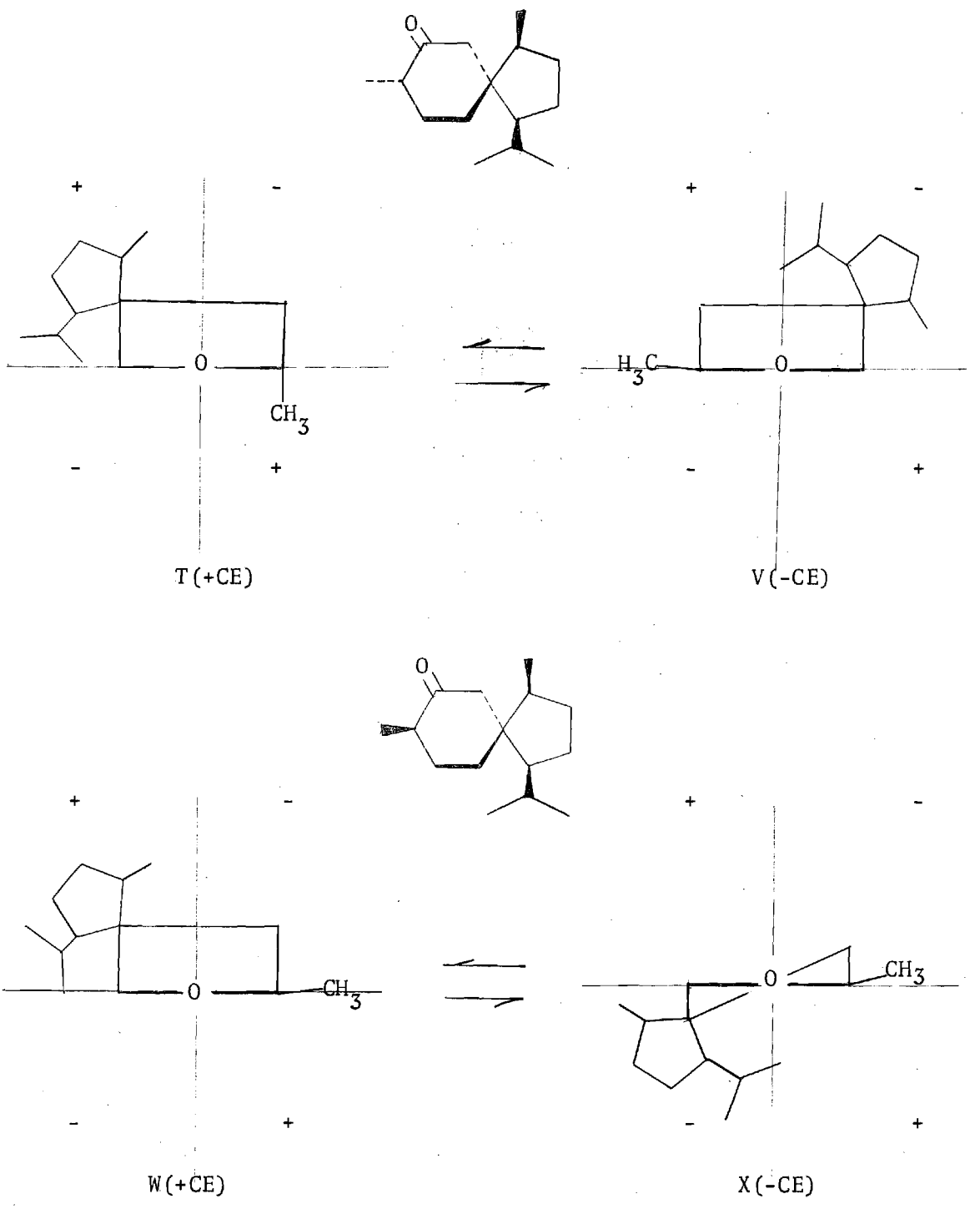


Figure 12. The Two Possible Epimers of 25 and Their Octant Projections.

between conformers such as T ⇌ V or W ⇌ X, which could account for these seemingly anomalous results. Proof of this conformational equilibrium could possibly be obtained by "freezing out" the more stable conformers with low temperature ORD and CD work. The ORD and CD spectra of 25a and 25b do not confirm or contradict the absolute configuration of 10 obtained by X-ray analysis due to the complexity of the system. It is interesting to note that the ORD and CD spectra of dihydroacorenone exhibited a weak negative Cotton effect (a -8.85).

The CD and ORD spectra of lactone 27 exhibited a positive Cotton effect (a +36). Klyne[88] has proposed a sector rule for lactones; however, this rule is not as reliable as the octant rule and is more ambiguous in its application. In addition to this, the conformation of the seven-membered lactone ring in 27 is quite flexible. Thus, no definitive information can be obtained from the ORD and CD of 27.

The ORD and CD spectra of the methyl ketone function of keto-ester 29 exhibited a weak negative Cotton effect (a -3.3) from which no definitive information about the configuration of 10 could be obtained.

Studies in the Synthesis of Acorenone-B

The general approach to the synthesis of acorenone-B (10) is given in Figures 13 and 14. The approach is to construct the five-membered ring of 10 with the methyl and isopropyl groups in the proper relationship, then build the basis for the six-membered ring. One advantage to this approach to the synthesis of acorenone-B (10) is that one of the intermediate compounds in the sequence is a degradation

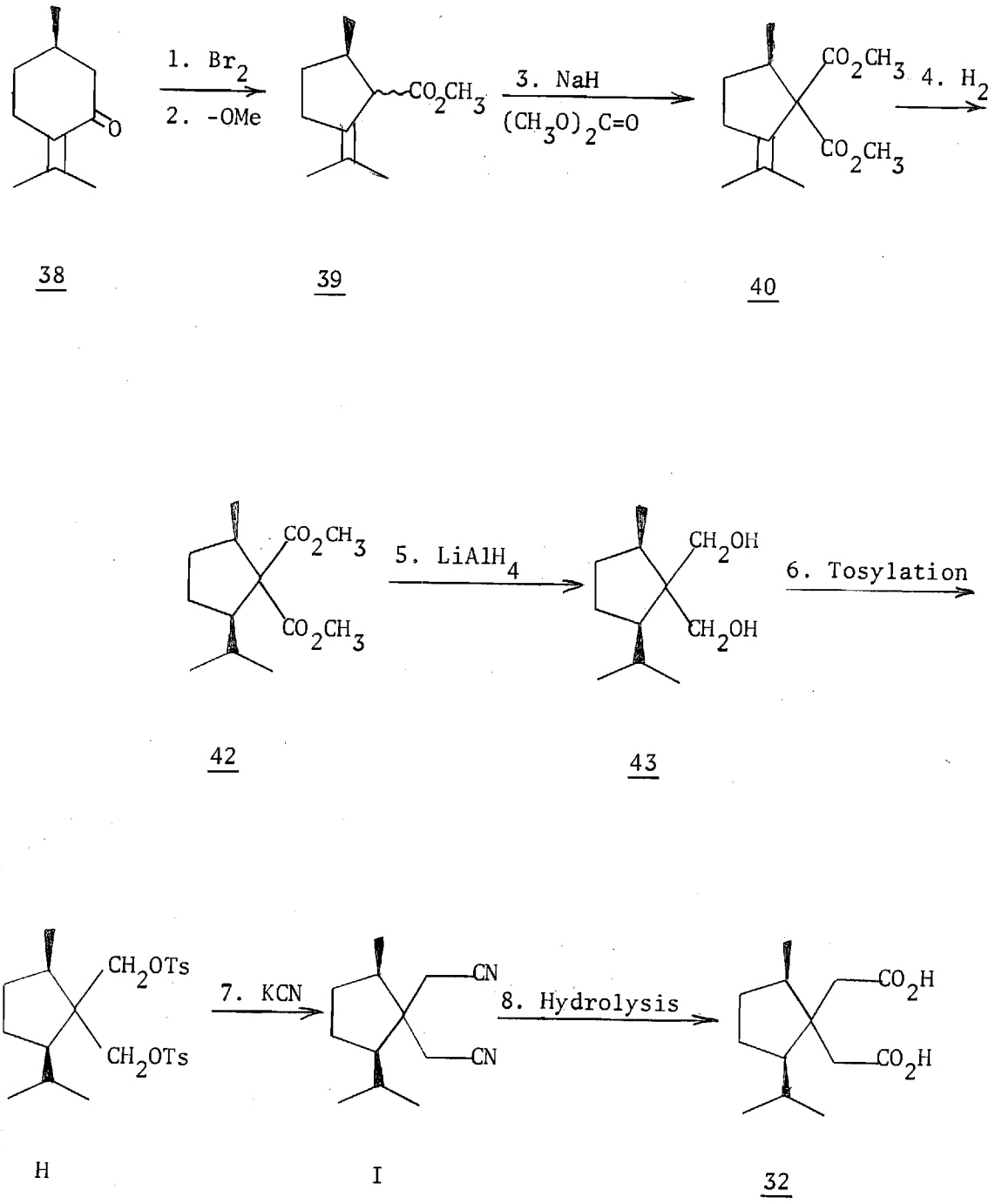


Figure 13. Approach to the Synthesis of the Dicarboxylic Acid Degradation Product (32) of Acorenone-B (10).

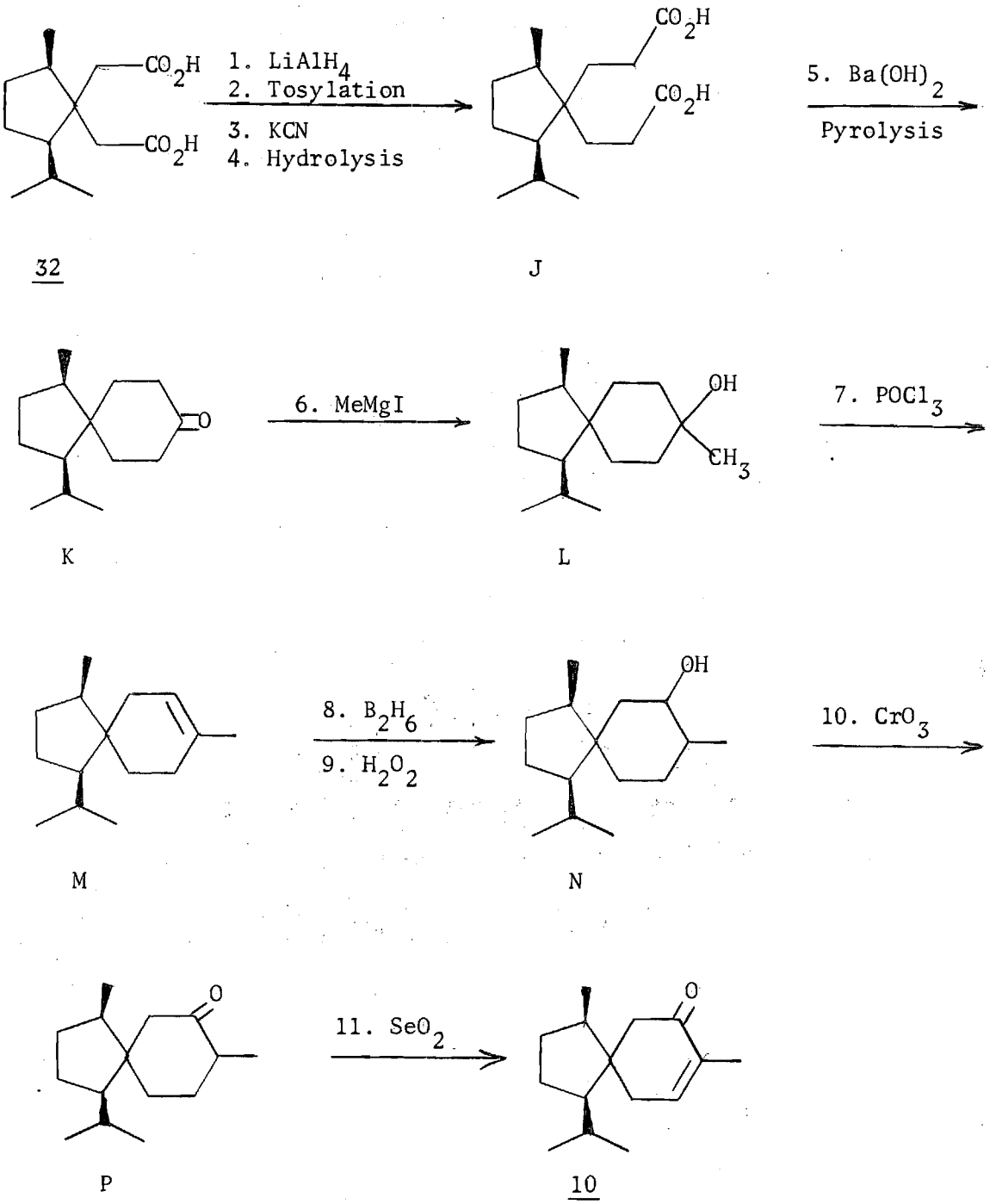


Figure 14. Approach to the Synthesis of Acorenone-B (10) Starting With the Dicarboxylic Acid Degradation Product (32).

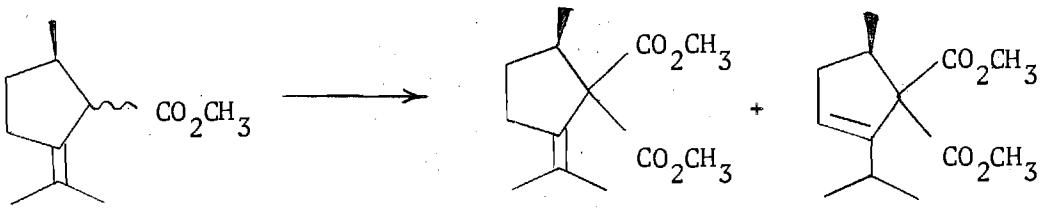
product of 10, namely, the diacid 32. It should also be noted that product M in Figure 14 should be a mixture of two compounds with different stereochemistry at the spirane junction; one compound should have the stereochemistry needed for the synthesis of 10, the other compound may have the stereochemistry needed for the synthesis of another sesquiterpene of the acorane type. Since both the coccinol ketone and acorenone (3) have been shown to be similar to acorenone-B (10), it is likely that one of these sesquiterpenes is the same as 10 except for the stereochemistry at the spirane juncture. Thus, the synthesis outlined in Figure 14 could possibly establish the structure of coccinol (9) or acorenone (3).

The starting material was pulegone (38), a readily available monoterpene. Methyl pulegenate (39) was prepared[66,67] by the Favorskii[66] rearrangement of the unstable dibromide of pulegone in the presence of sodium methoxide. The methyl pulegenate obtained in this manner was found to be a 1:1 cis,trans ratio to be GLC analysis and by comparison of the n.m.r. spectrum of the mixture (39) with the reported[66] n.m.r. spectra of cis and trans methyl pulegenate. The 1:1 cis,trans mixture was treated with dimethyl carbonate and sodium hydride. Approximately 80 percent of the reaction mixture was identified as unreacted cis and trans methyl pulegenate and products with similar retention times, presumably isomerized methyl pulegenate. The remaining 20 percent of the reaction mixture contained four products, two of which were isolated pure by column chromatography and identified as condensation products.

The compound which was first eluted from the column chromatography was assigned structure 41 ($C_{13}H_{20}O_4$) partly on the basis of its n.m.r. spectrum. The n.m.r. spectrum of 41 showed an olefinic proton as a triplet (337 cps, J=2 cps), two methylester groups as singlets (216 and 218 cps, $W_{1/2}$ = 1 cps), and three doublets (56, 58, and 64 cps, J=7 cps) for the secondary methyl groups. The infrared spectrum showed an absorption at 1725 cm^{-1} for the ester carbonyl.

The compound which was eluted from the column chromatography after 41 was assigned structure 40 ($C_{13}H_{20}O_4$) partly on the basis of its n.m.r. spectrum. The n.m.r. spectrum of 40 showed two methyl ester groups as singlets (219 and 221 cps), one secondary methyl as a doublet (60 cps, J=7 cps) and two methyl groups attached to a double bond at 95 and 101 cps respectively. The appearance of two signals showed that the signal at 95 cps had a larger coupling constant (J=2 cps) than the signal at 101 cps (J=0.5 cps). Bhacca and Williams[78] report that transoid coupling between the methyl protons of an isopropylidene group and the adjacent methylene protons is greater than the corresponding cisoid coupling in a steroid case. Thus, the C_9 methyl protons are assigned to the signal at 95 cps and the C_8 methyl protons are assigned to the signal at 101 cps. The carbomethoxy groups appear to have a shielding effect on the C_9 protons relative to the C_8 protons. The infrared spectrum of 40 showed an ester carbonyl absorption at 1725 cm^{-1}.

Further proof of the structures of both 40 and 41 came from their hydrogenation products. GLC analysis, under several different conditions, of the hydrogenation products of both 40 and 41 showed



39 40 41

only one peak, mixed injection of hydrogenated 40 and 41 also showed only one peak. The n.m.r. spectra and infrared spectra of hydrogenated 40 and 41 were superimposable. The hydrogenation of 40 and 41 gave the same compound, 42, which supports the postulation that 40 and 41 were double bond isomers. Since the hydrogenation gave only one compound, the hydrogenation was stereospecific. Examination of Dreiding models shows that the methyl group attached to the cyclopentane ring of 40 and 41 probably prevents hydrogenation from that side, thus giving rise to a cis relationship of the methyl group and isopropyl group of the cyclopentane ring which is required for the synthesis of acorenone-B (10). The infrared spectrum of 42 showed an ester carbonyl band at 1725 cm^{-1}. The n.m.r. spectrum of 42 showed three secondary methyl groups as doublets (51, 53.5, and 64 cps, J=6 cps) and one signal at 221 cps ($W_{1/2}$ = 2 cps) for the two methyl ester groups. The mass spectrum of 42 confirmed the molecular weight (242) of 42 and a peak at M^+ -31 (27%) indicated the presence of a methyl

ester by the loss of an O-CH_3 fragment.

Reduction of diester 42 with lithium aluminum hydride gave the alcohol 43. The infrared spectrum of 43 showed strong hydroxyl absorption at 3350 cm^{-1} and the absence of carbonyl absorption. The n.m.r. spectrum of 43 showed three secondary methyl groups as doublets (53, 59, 64 cps, J=6 cps), two hydroxyl protons as a broad singlet (170 cps) which disappeared when D_2O was added, a singlet for one of the C–CH_2–O groups (224 cps, $W_{1/2}$ = 1.5 cps), and a doublet of doublets for the other C-CH_2-O group (203, 214, 221, 232 cps, J=11 cps). The alcohol (43) was somewhat unstable upon distillation. The lack of material at this point prevented the continuation of the synthetic approach as outlined in Figure 13.

The low yield of the condensation products 40 and 41 from the reaction of 39 with sodium hydride and dimethyl carbonate was not unexpected because of the presence of the double bond adjacent to the carbanion formed. It was not determined experimentally whether isomerization of the double bond in 41 took place before or after the condensation with dimethyl carbonate. Other condensation products were probably formed, but only the main condensation products 40 and 41 were isolated and characterized. The low yield of 40 and 41, coupled with the erratic nature of the reaction prompted an investigation of other methods of obtaining the desired condensation products.

Methyl pulegenate (39) was hydrogenated to yield a mixture of two saturated compounds (44) of undetermined stereochemistry. The sodium hydride-dimethyl carbonate condensation was attempted with 44, but only a trace of the desired condensation product was obtained.

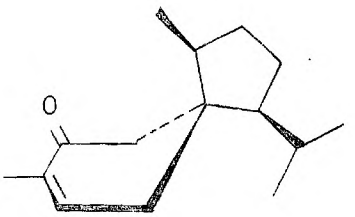
The reaction mixture was refluxed for an extended period of time resulting in the reduction of 44 to an alcohol. Fieser and Fieser[37] have reported that ketones which have no α-hydrogens are reduced by sodium hydride. The hydrogen alpha to the carbomethoxy group is either not acidic enough to be removed or sterically inaccessible, thus leading to the reduction of the carbomethoxy group by sodium hydride.

A different base, trityl lithium, was used to form the carbanion of 39 and methyl chloroformate was used in place of dimethyl carbonate. Although the formation of the anion of 39 was indicated by a color change, the desired condensation products 40 or 41 were not detected by GLC analysis. Thus, the investigation of different routes to 40 or 41 did not lead to any improvement over the sodium hydride-dimethyl carbonate condensation reaction.

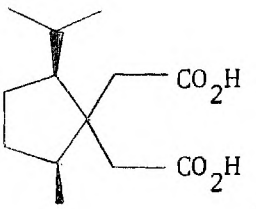
CHAPTER V

CONCLUSIONS

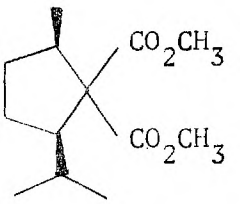
The structure of a new spiro sesquiterpene of the acorane type, acorenone-B (10), has been established by X-ray analysis of its 4-iodo-2-nitrophenylhydrazone derivative. The chemical degradation of acorenone-B (10) fully supports the assigned structure. Acorenone-B (10) has



10



32



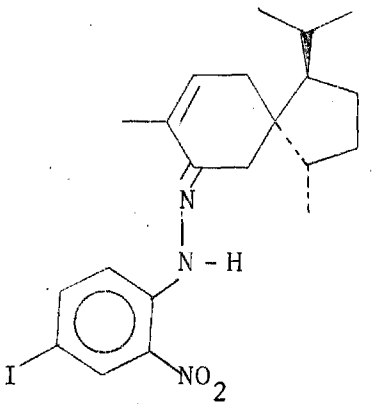
43

been shown to be different from the previously reported acorenone (3) to which Sorm et al.[5] assigned the same gross structure as 10 without assigning the stereochemistry. On the basis of the comparison of melting points and infrared spectra, the ozonolysis products of acorenone-B and acorenone were both assigned structure 32, implying that acorenone has the same stereochemistry as 10 except for the stereochemistry at the spirane carbon juncture. However, conclusive proof of the structure of Sorm's acorenone (3) can only be obtained by direct comparison of the ozonolysis products (32) from acorenone (3) and acorenone-B (10).

Acorenone-B (10) has been shown to be different from the coccinol ketone reported by Arigoni.[20] However, the similarity of the infrared and n.m.r. spectra of acorenone-B (10) and the coccinol ketone suggests that coccinol (9) has the acorane type of hydrocarbon skeleton.

The absolute configuration of acorenone-B (10) has been determined by X-ray analysis of acorenone-B 4-iodo-2-nitrophenylhydrazone (36). Attempts to verify this assignment by ORD and CD studies of acorenone-B and its degradation products have been hindered by the apparent complexity and the conformational equilibrium shown by these compounds.

An approach to the synthesis of acorenone-B has been developed with the synthesis of the key five-membered ring intermediate 43. The condensation reaction of methyl pulegenate with dimethyl carbonate is erratic and goes in a low yield; however, this reaction is early in the synthetic sequence and the starting material is readily available.



36

CHAPTER VI

RECOMMENDATIONS

The structure of Sorm's acorenone could be established by converting the small amount of authentic dihydroacorenone on hand to acorenone. Methods for this conversion should first be worked out using dihydroacorenone-B. This conversion would also be useful in the synthesis of acorenone-B. The acorenone obtained in this manner should be ozonized and the ozonolysis product directly compared with the ozonolysis product of acorenone-B.

Low temperature and solvent dependency ORD and CD studies of the two pure epimers of dihydroacorenone-B should be made in order to confirm the suspected conformational equilibrium present in these compounds.

The synthesis of acorenone-B should be continued as outlined in Figures 13 and 14 of Chapter IV. Although the yield of the condensation of methyl pulegenate and dimethyl carbonate is not high, large scale reactions should provide enough of the required condensation product for the continuation of the synthesis.

APPENDIX

The reported quantities for the ORD measurements[34] were calculated as shown in equations 1-4, where α_{253} is the rotation at 253 mμ, $[\alpha]_{253}$ is the specific rotation at 253 mμ, and $[\Phi]_{253}$ is the molecular rotation at 253 mμ.

The molecular amplitude, a, is defined as the difference between the molecular rotation at the extremum (peak or trough) of the longer wavelength $[\Phi]_1$, and the molecular rotation at the extremum of shorter wavelength $[\Phi]_2$, divided by 100.

$$\alpha_{253} = \text{(instrument scale in degrees) x (chart measurement)} \quad (1)$$

$$[\alpha]_{253} = \frac{100 \times \alpha_{253}}{\text{(conc. in gm/100 ml) x (pathlength of transmitted light in dm)}} \quad (2)$$

$$[\alpha]_{253} = \frac{[\alpha]_{253} \times \text{(mol. wt.)}}{100} \quad (3)$$

$$a = \frac{[\Phi]_1 - [\Phi]_2}{100} \quad (4)$$

The reported quantities for the CD measurements[34] were calculated as shown in equation 5. The quantity Γ is the width of the peak at its half height and Θ is the molecular elipticity.

$$[\Theta] = \frac{3300 \text{ (scale)} \times \text{(chart measurement)}}{\text{(conc. in moles/liter) (pathlength of transmitted light in cm)}} \quad (5)$$

The theoretical correllation between molecular amplitude, a, and molecular ellipticity is given by equation 6.

$$a = 0.0122 \times [\Theta] \quad (6)$$

The calculation of relative positions, $\Delta\nu_{AB}$, of the absorption positions (in cps) for an AB n.m.r. spectrum[72] is given by equations 7-8, where !,2,3,4 are the chemical shifts of the n.m.r. peaks 1,2,3,4 respectively (in cps) and J_{AB} is the coupling constant obtained by $J_{AB} = |1\text{-}2| = |3\text{-}4|$.

$$|1 - 3| = |2 - 4| = \left(\Delta\nu_{AB}^2 + J_{AB}^2\right)^{1/2} \quad (7)$$

$$[(1\text{-}3)^2 - J_{AB}^2]^{1/2} = \Delta\nu_{AB} \quad (8)$$

The relative intensities, i, of the peaks of an AB n.m.r. spectrum are given by equation 9-10. The ratio of intensities

$$i_1 = i_4 = 1 - \frac{J_{AB}}{(\Delta\nu_{AB}^2 + J_{AB}^2)^{1/2}} \quad (9)$$

$$i_2 = i_3 = 1 + \frac{J_{AB}}{(\Delta\nu_{AB}^2 + J_{AB}^2)^{1/2}} \qquad (10)$$

is calculated by i_1/i_2 or i_4/i_3.

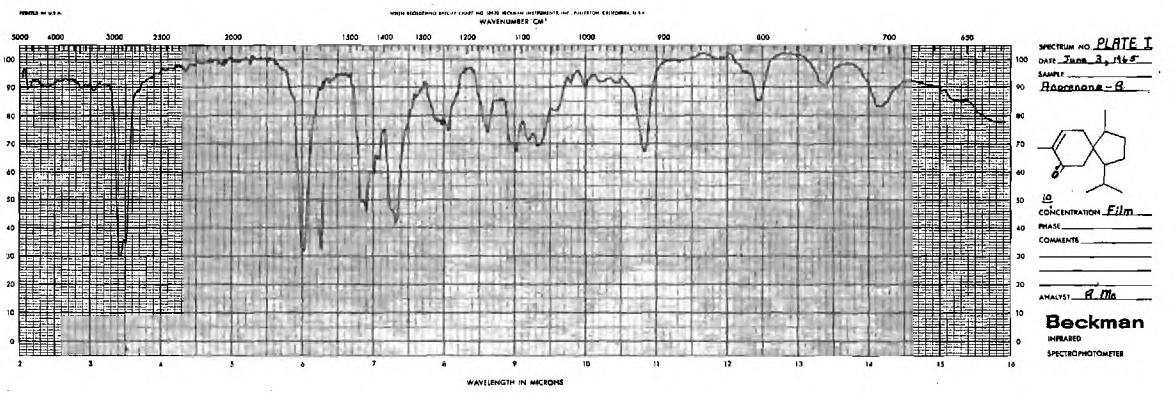


Plate I. Infrared Spectrum of Acorenone-B (10).

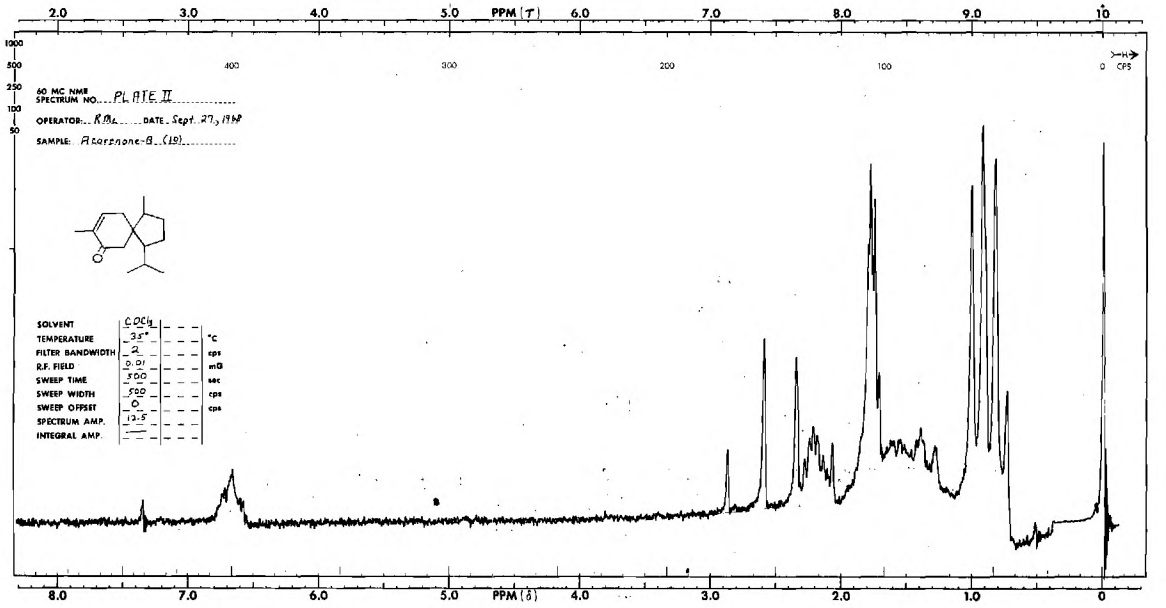


Plate II. N.M.R. Spectrum of Acorenone-B (10).

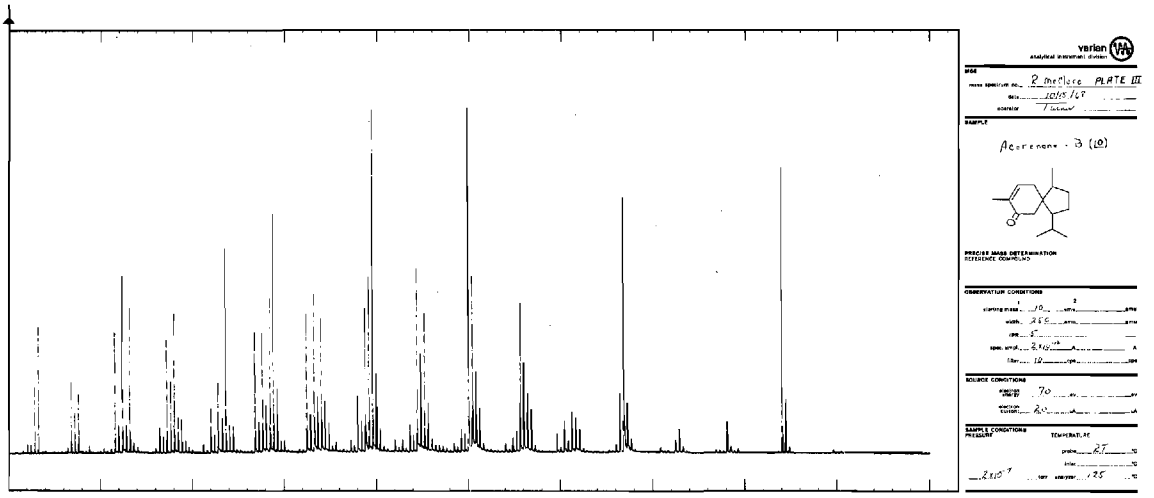


Plate III. Mass Spectrum of Acorenone-B (10).

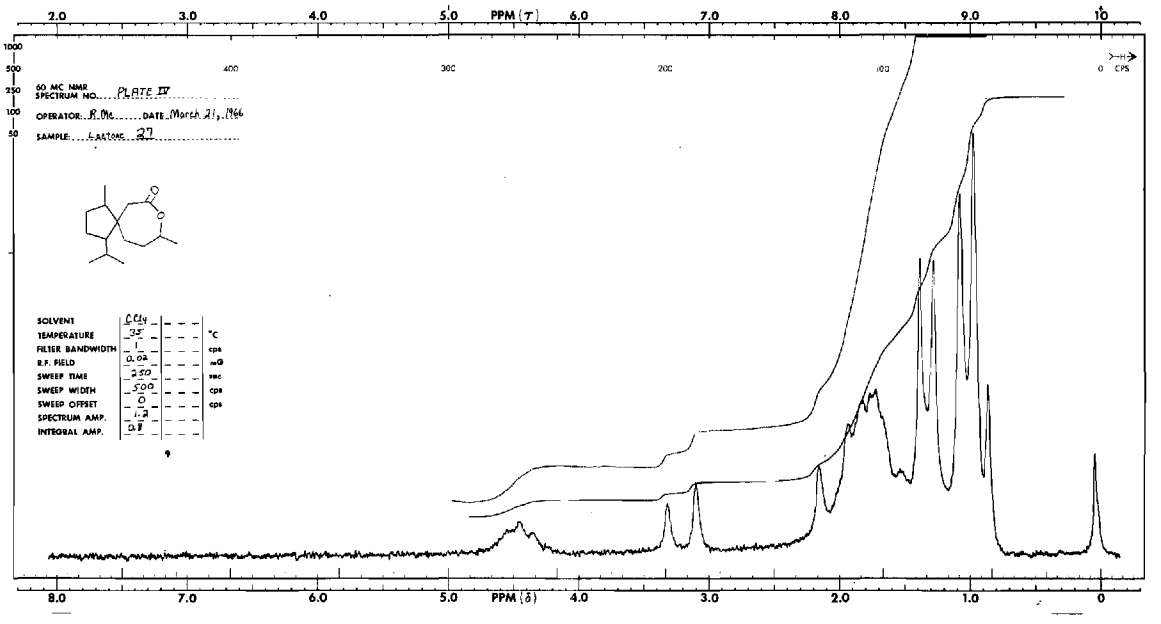


Plate IV. N.M.R. Spectrum of Lactone 27.

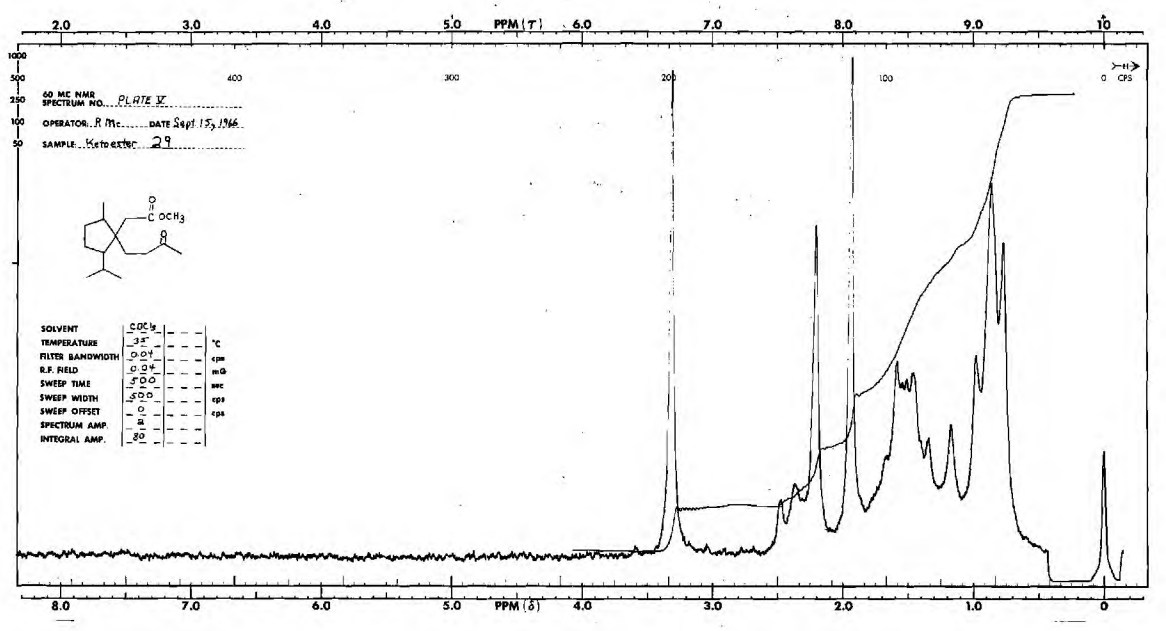


Plate V. N.M.R. Spectrum of Ketoester 29.

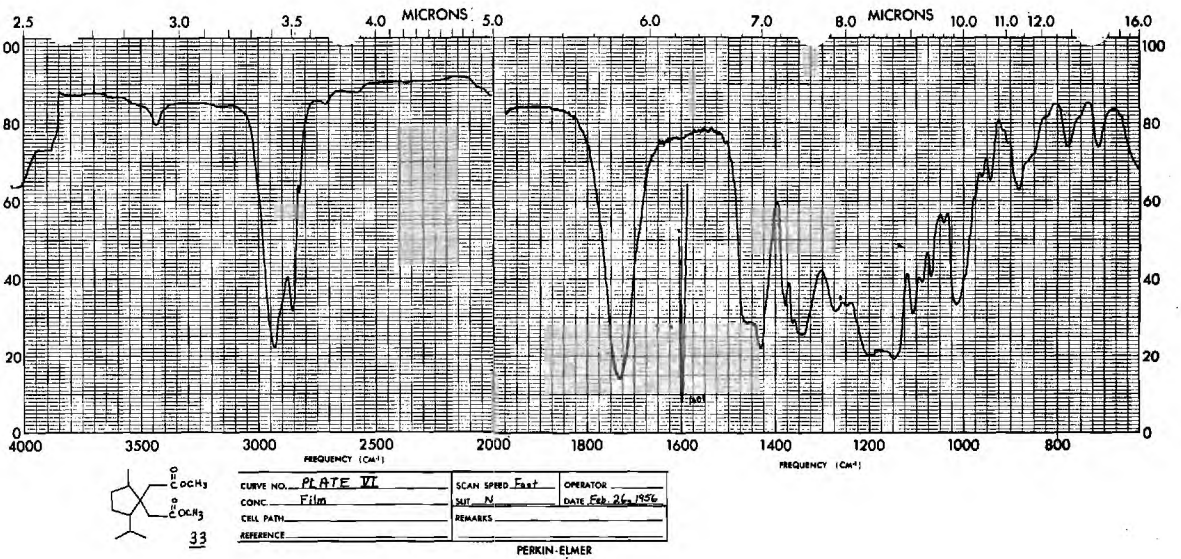


Plate VI. Infrared Spectrum of Diester 33.

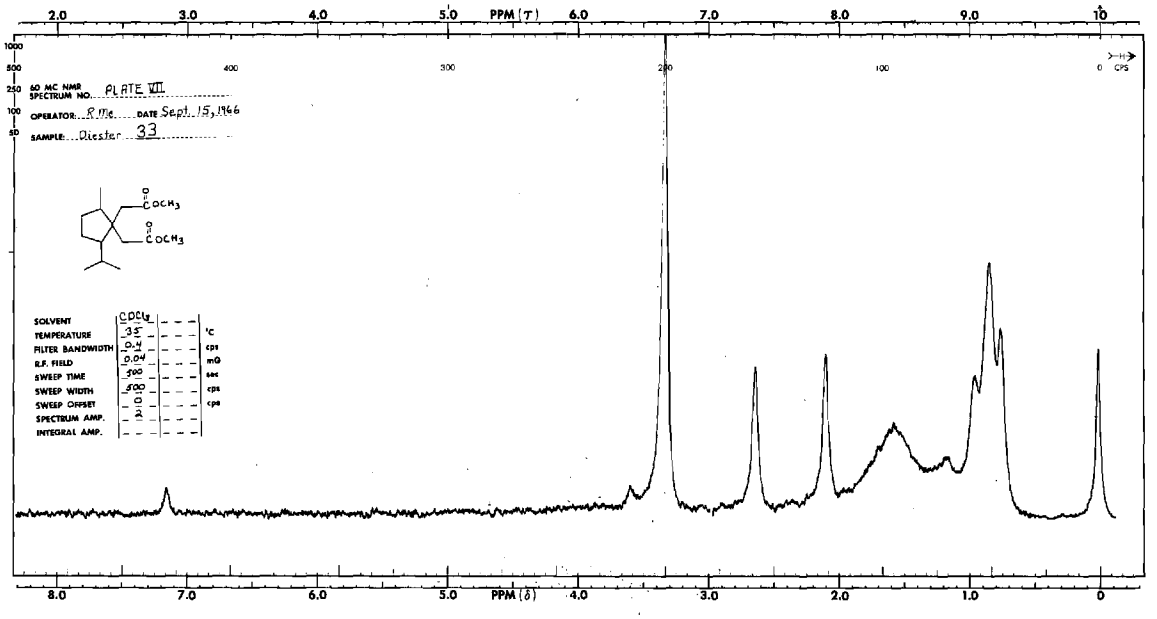


Plate VII. N.M.R. Spectrum of Diester 33.

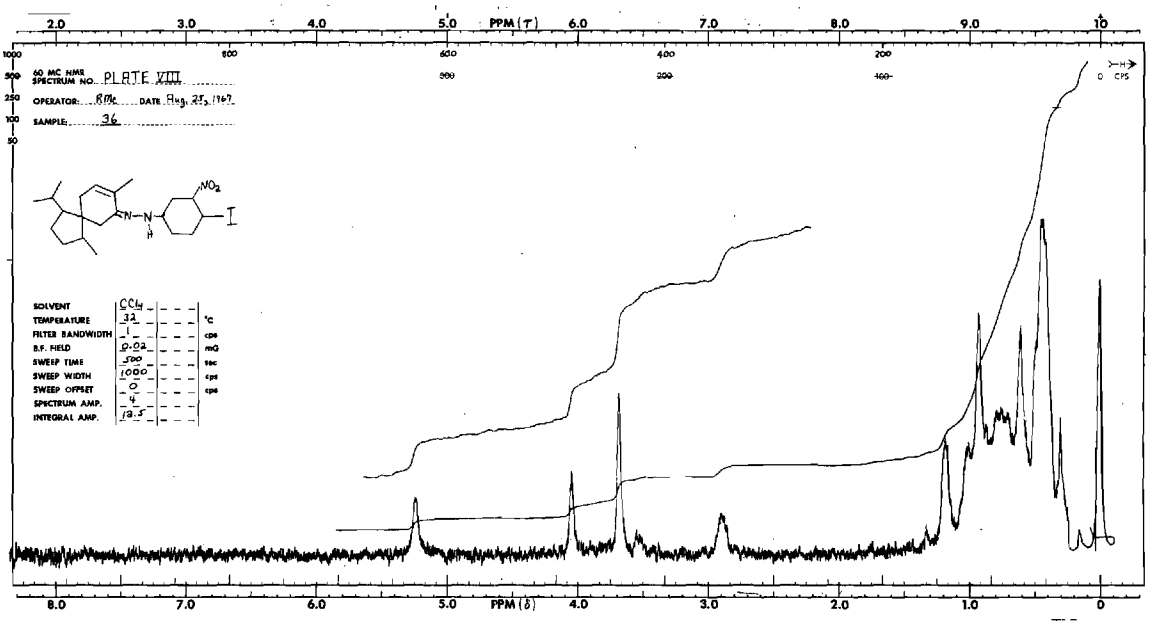
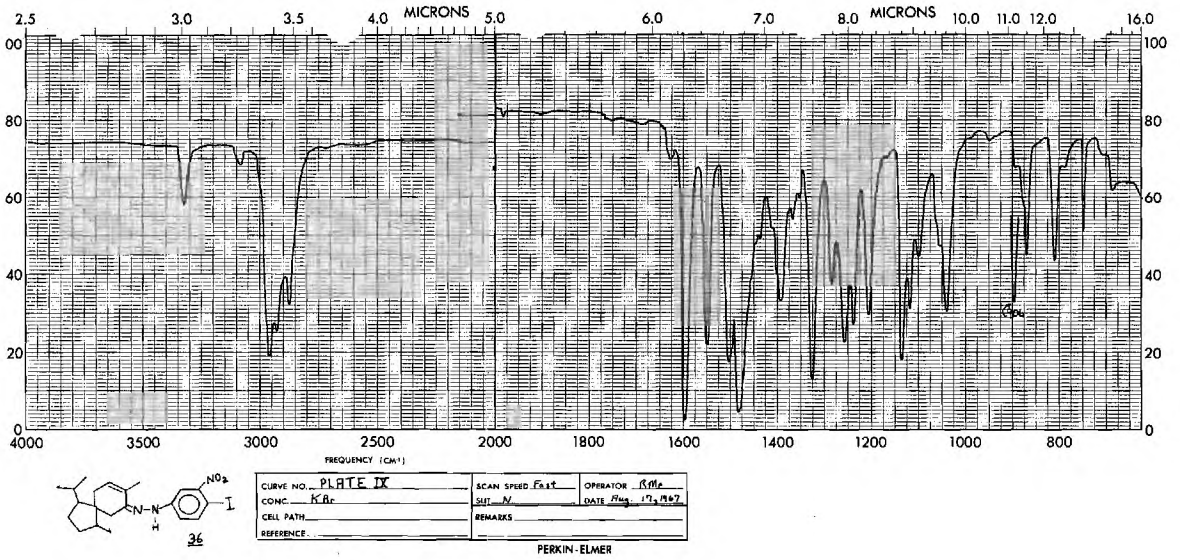


Plate VIII. N.M.R. Spectrum of 36.



36

Plate IX. Infrared Spectrum of 36.

BIBLIOGRAPHY*

1. L. H. Zalkow, V. B. Zalkow and D. R. Brannon, Chem. Ind. (London), 38 (1963).

2. G. L. Chetty, V. B. Zalkow and L. H. Zalkow, Tetrahedron Letters, 3223 (1968).

3. V. B. Zalkow, A. M. Shaligram and L. H. Zalkow, Chem. Ind. (London) 194, (1964).

4. J. Vrkoc, V. Herout and F. Sorm, Collection Czechoslov. Chem. Commun., 26, 1021 (1961).

5. J. Vrkoc, V. Herout and F. Sorm, Collection Czechoslov. Chem. Commun. 26, 3183 (1961).

6. K. S. Schorno, Ph.D. Thesis, Oklahoma State University, pp. 1-26.

7. E. J. Corey, M. Ohno, R. B. Mitra and P. A. Vatakencherry, J. Am. Chem. Soc., 86, 478 (1964).

8. L. Ruzicka, Experientia, 9, 357 (1953).

9. W. Parker and J. S. Roberts, Quart. Rev. (London), 331 (1967).

10. V. Sykora, V. Herout, J. Pliva and F. Sorm, Chem. Ind. (London), 1231 (1956).

11. F. Sorm and V. Herout, Collection Czechoslov. Chem. Commun., 13 177 (1948).

12. F. Sorm and V. Herout, Collection Czechoslov. Chem. Commun., 14, 724 (1949).

13. V. Sykora, V. Herout, J. Pliva and F. Sorm, Collection Czechoslov. Chem. Commun., 23, 1072 (1958).

14. V. Sykora, V. Herout, A. Reiser and F. Sorm, Collection Czechoslov. Chem. Commun., 24, 1306 (1959).

---

*Journal title abbreviations used are listed in "Index of Periodicals," Chemical Abstracts, 55 1 J (1961).

15. J. Vrkoc, V. Herout and F. Sorm, Collection Czechoslov Chem. Commun., 27, 2709 (1962).

16. J. Vrkoc, V. Herout and F. Sorm, Collection Czechoslov. Chem. Commun., 28, 1084 (1963).

17. J. Vrkoc, V. Herout and F. Sorm, Collection Czechoslov. Chem. Commun., 29, 539 (1964).

18. C. E. McEachan, A. T. McPhail and G. A. Sim, Chem. Commun., 276 (1965).

19. G. Ourisson, S. Munavalli and C. Ehret, "International Tables of Selected Constants 15 Data Relative to Sesquiterpenoids," Permagon Press, New York, 1966, p. 9.

20. D. Arigoni, private communication, Sept. 23, 1968.

21. A. J. Birch, F. A. Hochstein, J. A. K. Quartey and J. P. Turnbull, J. Chem. Soc., 2923 (1964).

22. J. M. Mellor and S. Munavalli, Quart. Rev. (London), 270 (1964).

23. K. R. Varma, M. L. Maheshwari and S. C. Bhattacharyya, Tetrahedron, 21, 115 (1965).

24. J. A. Marshall, N. H. Andersen and P. C. Johnson, J. Am. Chem. Soc., 89, 2748 (1967).

25. J. Simonsen and D. H. R. Barton, "The Terpenes," Vol. III, Cambridge University Press, London, 1952, pp. 224-232.

26. J. A. Marshall and P. C. Johnson, J. Am. Chem. Soc., 89, 2750 (1967).

27. J. A. Marshall and P. C. Johnson, Chem. Commun., 391 (1968).

28. W. Z. Chow, O. Motl and F. Sorm, Collection Czechoslov. Chem. Commun., 27, 1914 (1962).

29. G. Chiurdoglu and J. Decot, Tetrahedron, 4, 1 (1958).

30. M. Romanuk and V. Herout, Collection Czechoslov. Chem. Commun., 25, 2540 (1960).

31. S. Ito, K. Endo, T. Yoshida, M. Yatagai and M. Kodama, Chem. Commun., 186 (1967).

32. Y. Ohta and Y. Hirosi, Tetrahedron Letters, 2483 (1968).

33. A. Tanaka, H. Uda and A. Yoshikoshi, Chem. Commun. 188 (1967).

34. P. Crabbe, "Optical Rotary Dispersion and Circular Dichroism in Organic Chemistry," Holden Day, San Francisco, 1965, p. 14-20.

35. P. Crabbe, private communication.

36. D. Henneberg and K. Casper, "Chemical Formulae for Mass Determination", Fried Krupp, Mulheim, West Germany, 1967.

37. L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," John Wiley and Sons, Inc., New York, 1967, pp. 142, 1080.

38. M. F. Hawthorne, W. D. Emmons and K. S. McCallum, J. Am. Chem. Soc., 80, 6395 (1958).

39. N. C. Crossley and H. B. Henbest, J. Chem. Soc., 4413 (1960).

40. H. Zinner, H. Brenken, W. Braun, I. Falk, E. Fechtner and E. Hakner, Ann. Chem., 622, 133 (1959).

41. R. J. W. Cremlyn, J. Chem. Soc., 1229 (1966).

42. G. Gaudemaris and J. E. Dubois, Bull. Soc. Chim. France, 63 (1950).

43. R. Hodges, S. G. McGeachin and R. A. Raphael, J. Chem. Soc., 2515 (1963).

44. M. P. Brenans and M. A. Haller, Compt. Rend., 135, 177 (1902).

45. S. S. Joshi and D. S. Deorha, J. Ind. Chem. Soc., 34, 14 (1957).

46. C. Willgerodt and E. Arnold, Chem. Ber., 34, 3343 (1901).

47. S. S. Joshi and D. S. Deorha, J. Ind. Chem. Soc., 38, 31 (1961).

48. R. S. Kapil, J. Chem. Soc., 4127 (1959).

49. M. J. Buerger, "The Precession Method," John Wiley and Sons, Inc., New York, 1964.

50. "International Tables for X-ray Crystallography," Vol. 1, Kynoch Press, New York, 1962, p. 104.

51. D. A. Carpenter, Ph.D. Thesis, Georgia Institute of Technology, Appendix (1968).

52. "International Tables for X-ray Crystallography," Vol. 3, Kynoch Press, New York, 1962, pp. 163-216.

53. M. J. Buerger, "Crystal-Structure Analysis," John Wiley and Sons, Inc., New York, 1960.

54. D. L. Plymale, Ph.D. Thesis, Georgia Institute of Technology, p. 138 (1966).

55. L. J. Gallaher and M. I. Kay, "A Translation of a Fortran Crystallographic Least Squares Program by W. R. Busing, K. O. Martin and H. A. Levy to Extended Algol." Georgia Institute of Technology, Technical Report No. 1, Project B-270, May 27, 1964.

56. A. Zalkin, Fortran Fourier Analysis Program, FORDAP.

57. D. W. Beard, "Goniostat Alignment Instructions," Picker Instruments, Cleveland, Ohio (1967).

58. F. Carter, "Master Card Program for the Picker Four-angle Programmer," Picker Instruments, Cleveland, Ohio (1967).

59. W. R. Busing, K. O. Martin and H. A. Levy, Fortran Crystallographic Least Squares Program, XFLS (Modified version of ORFLS), Oakridge National Laboratories.

60. G. N. Ramachandran (editor), "Advanced Methods of Crystallography," Academic Press, New York, 1964, p. 67.

61. W. C. Hamilton, Acta Cryst., 18, 502 (1965).

62. A. Cooper and D. A. Norton, Acta Cryst., B 24, 811 (1968).

63. F. H. Allen, S. Neidle and D. Rogers, Chem. Commun., 308 (1968).

64. A. F. Peerdeman, A. J. Van Bommel and J. M. Bijvoet, Proc. Koninkl. Ned. Akad. Wetenschap., 52, 313 (1951).

65. E. Guenther and D. Althausen, "The Essential Oils," Vol. 2, D. Van Nostrand Company, Inc., New York, 1949, p. 400.

66. J. Wolinsky and D. Chan, J. Org. Chem., 30, 41 (1965).

67. S. A. Achmad and G. W. K. Cavill, Aust. J. Chem., 16, 858 (1963).

68. E. J. Corey, R. B. Mitra and H. Uda, J. Am. Chem. Soc., 86, 485 (1964).

69. J. Huff, Ph.D. Thesis, Georgia Institute of Technology, pp. 18-20 (1968).

70. M. Horak, O. Motl, J. Pliva and F. Sorm, "Die Terpene", Teil 2, Akademie-Verlag, Berlin, 1963.

71. N. S. Bhacca, L. F. Johnson and J. N. Shoderg, "High Resolution NMR Spectra Catalog", Vol. 1, Varian Associates (1962), spectra 271,275.

72. J. R. Dyer, "Applications of Absorption Spectroscopy of Organic Compounds", Prentice-Hall, Inc., Englewood Cliffs, N. J., 1965, p. 102.

73. R. McClure, K. S. Schorno, J. A. Bertrand and L. H. Zalkow, Chem. Commun., 1135 (1968).

74. "UV Atlas of Organic Compounds", Vol. 2, Butterworths, London, 1966, spectrum B 3/5.

75. J. Pliva, M. Horak, V. Herout and F. Sorm, "Die Terpene", Teil 1, Akademie-Verlaz, Berlin, 1960.

76. C. H. Hassall, "Organic Reactions", John Wiley and Sons, New York, 1957, p. 73.

77. S. L. Friess and P. E. Frankenburg, J. Am. Chem. Soc., 74, 2679 (1952).

78. N. S. Bhacca and D. H. Williams, "Applications of N.M.R. Spectroscopy in Organic Chemistry," Holden Day, Inc., 1964, pp. 37-38, 111.

79. W. R. Busing, K. O. Martin and H. A. Levy, Fortran Function and Error Program, OR FFE, Oak Ridge National Laboratories.

80. Y. L. Oh and E. N. Maslen, Acta Cryst., B24, 883 (1968).

81. C. K. Johnson, A. Fortran Thermal-Ellipsoid Plot Program for Crystal Structure Illustrations, ORTEP, Oak Ridge National Laboratory (1965).

82. J. A. Bertrand, Fortran Program for Calculating Equations of Planes by the Least-Squares Technique, (1968).

83. J. W. Moncrief and W. N. Lipscomb, Acta Cryst., 21, 322 (1966).

84. C. Djerassi, R. Records, E. Bunnenberg, K. Mislow and A. Moscowitz, J. Am. Chem. Soc., 84, 870 (1962).

85. K. Kiriyama, M. Moriyama, T. Iwata and K. Tori, Tetrahedron Letters, 1661 (1968).

86. G. Snatzke, "Optical Rotary Dispersion and Circular Dichroism in Organic Chemistry", Sadtler Research Laboratories, Inc., Philadelphia, 1967, p. 340.

87. K. M. Wellman, W. S. Briggs and C. Djerassi, J. Am. Chem. Soc., 87, 73 (1965).

88. J. P. Jennings, W. Klyne and P. M. Scopes, J. Chem. Soc., 7211 (1965).

VITA

Richard J. McClure, Jr., was born in Goessel, Kansas on December 2, 1942. He attended elementary and high school in Peabody, Kansas, where he received his high school diploma in May, 1960. In September of the same year, he began undergraduate study at Southwestern College in Winfield, Kansas, where in June, 1964 he received the degree of Bachelor of Arts in Chemistry and Mathematics.

In June, 1964 he began graduate study in organic chemistry with Dr. Leon H. Zalkow at Oklahoma State University, Stillwater, Oklahoma. He continued his graduate study at Georgia Institute of Technology, Atlanta, Georgia in September, 1965, after Dr. Zalkow's move to the same institution.

Richard is married to the former Marjorie Kay Harp and is the father of two sons: Mark A. and Brian S. McClure.

Richard has been awarded a postdoctoral National Cancer Institute fellowship for study under Professor George A. Sim at the University of Sussex, Brighton, England in the field of X-ray analysis of biologically active compounds.